VOLUME [illegible] NUMBER 2

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AUGUST 1935

PUBLISHED [illegible] AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN [illegible] CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $[illegible]

Entered at [illegible] 1917, at the Postoffice at Chicago, Illinois, under Act of Congress [illegible] Acceptance for mailing at special rate of postage provided for [illegible] Act of Oct. 3, 1919, authorized July 29, 1918.

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Archives of Dermatology and Syphilology

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UNUSUAL CUTANEOUS SYMPTOMS ASSOCIATED WITH RETENTION OF ARSENIC

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AND
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NEW YORK

About ten years ago we observed a patient with unusual lesions of the skin. In view of the fact that these lesions differed in so many aspects from those already described in the literature, an attempt was made to investigate the cause and relation of the lesions to the treatment which the patient had previously received. In the course of this study several other patients with similar conditions were found, and comment on these patients is presented here.

The first patient showing these symptoms was a man with dermatitis herpetiformis, to whom arsenic had been administered in large amounts. A synopsis of his case was given in a previous paper, entitled "The Use of Sodium Thiosulphate in Diagnostic Procedure." [1] Another patient gave a history of arsenical medication, but two others gave no history of this therapy. A fifth patient presented marked pigmentation from occupational contact with substances containing arsenic.

These cases are of sufficient interest to justify a more complete review.

REPORT OF CASES

CASE 1.—H. S., a Roumanian Jew, 39 years of age, who had been in the United States for twenty-four years, was first seen on Dec. 20, 1923. He had been suffering with Duhring's disease for four years. The clinical picture was typical, and for two years he had been taking arsenic in the form of pills, for the previous four months averaging nine pills a day. He remained in the hospital until March 1924, receiving solution of potassium arsenite up to 18 minims (1.098 cc.) three times a day. After leaving the hospital he went to another dispensary, where he was given more arsenic in the form of pills. He took two hundred of these in the next two months. During these two months his skin became more and more pigmented. He was next seen by one of us (T.) at his home in September 1924, and he returned to the hospital. He claimed that he had taken no arsenic for the previous two months. He was acutely ill and suffered with hemorraghic diarrhea for several days. The skin of his entire body was deeply pigmented. Around the mouth, neck and genitals there was an exudative dermatitis covered with greenish pus. Culture showed that this was due to a superadded infection

1. Myers, C. N.; Marples, E.; Groehl, M., and Throne, B.: The Use of Sodium Thiosulphate in Diagnostic Procedure, J. Lab. & Clin. Med. **11**:836 (June) 1926.

with Staphylococcus citreus. The pigmented skin was covered with follicular papulovesicles, was edematous and thickened and showed considerable exudation. As the exudation ceased, the papules became lichenoid but were acuminate. In places they were confluent, and there were elevated lesions resembling the granulomas seen in mycosis fungoides. These lesions, covered with an unbroken skin, were most marked at the base of the neck and over the shoulders, although many others were scattered over the trunk and limbs. During periods of quiescence the vesicular character of the follicular lesions would disappear, leaving acuminate papules seated on a very dark skin, which from treatment had become much less infiltrated. Examination of the urine showed a large number of granular casts and some albumin. The specific gravity was normal. The patient left the hospital on Feb. 28, 1925, but shortly after he was readmitted to another hospital, where he was given injections of sodium cacodylate which caused an exacerbation. On discharge from our service he was markedly improved. After discharge from the second hospital he went to several others, among which was the Montefiore Hospital, New York.

A biopsy on admission to the hospital with which we are associated showed that the epidermal pegs were lengthened and in some cases forked at the base. In places the papillary plates were very thin. The epidermal cells showed some mitotic figures, and pigment was present. The blood vessels were dilated throughout, and the perivascular infiltration, which was especially marked in the hypoderm, was composed almost entirely of plasma cells. A diagnosis of chronic inflammation was made.

A biopsy was performed at the Montefiore Hospital on March 8, 1927. The clinical diagnosis was mycosis fungoides or lymphoblastoma. Bits of skin showed marked hypertrophy of the papillae, and in the corium there were irregular nests of polygonal and round cells, numerous leukocytes and occasional eosinophils. There were scattered deposits of yellowish-brown pigment. The diagnosis was chronic granuloma of the skin.

The results of hematologic examination at the Montefiore Hospital was as follows: hemoglobin (Sahli), 80 per cent; erythrocytes, 4,900,000; leukocytes, 9,500; polymorphonuclears, 72.5 per cent; lymphocytes, 14.1 per cent; large mononuclears and transitionals, 2 per cent; eosinophils, 3.5 per cent; basophils, 0.5 per cent; myelocytes, 7 per cent.

A letter received from the patient from Hot Springs, Ark., dated Oct. 23, 1929, stated that he was "90 per cent well." During his stay at Hot Springs he was seen by Dr. Lautman, who diagnosed the condition as dermatitis herpetiformis, and by Dr. Menage, of New Orleans, who made a diagnosis of lichen planus (letter from Dr. W. H. Deadrick).

Between Sept. 25, 1924, and Feb. 19, 1925, twenty-five urinalyses were made for arsenic. The amounts of arsenic found varied from 0.0 to 2.63 mg. per hundred grams of dried substance. Two specimens of blood were also examined for arsenic. One showed a trace, and the other was normal. The photographs show the marked edema of the face and the follicular lichenoid papules (figs. 1 and 2).

Case 2.—M. C., aged 7 years, an American girl born of Italian parents, was admitted to the outpatient department on July 27, 1921. She had suffered since infancy with a condition diagnosed as eczema. It was very widespread, involving the face, trunk and limbs. She was not seen again until Jan. 17, 1922. After that her attendance for a while was very irregular, and then she was not seen again until Nov. 3, 1924. At this time her whole body was deeply pigmented and showed the same type of follicular papulovesicles as those described in case 1. The same granulomatous lesions were present on the shoulders, back and base of the neck.

A biopsy was made and the section showed a fairly normal epidermis, well marked rete pegs and slight parakeratotic scaling. There was a large amount of

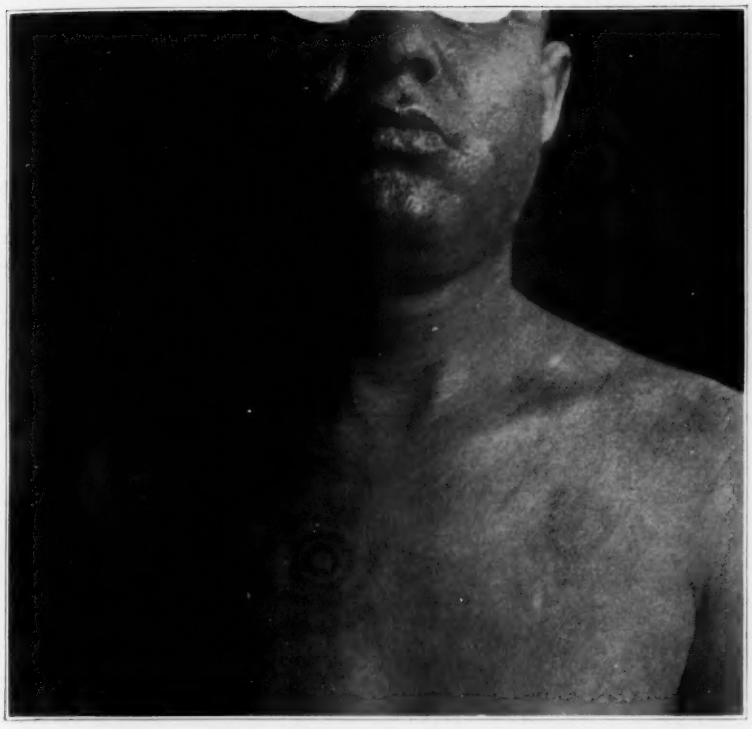

Fig. 1 (case 1).—Photograph showing the edema of the skin, the pigmentation and on the right shoulder and arm a few of the granulomatous lesions.

Fig. 2 (case 1).—View showing follicular papules, some granulomatous lesions and the white centers of the lesions. The photograph was taken after the patient had been under treatment. When first seen the pigmentation was uniform.

pigment in the lower layers of the epidermis. There was some pigment in the corium as well. Islands of cellular exudate were scattered throughout the corium. They were of varying size, but the cells were always large and pale rather than lymphocytic. The endothelium of the blood vessels was swollen. A diagnosis of chronic inflammation was made.

Her attendance was fairly regular for a short time, and by March 18, 1925, the pigmented lichenoid condition showed considerable improvement. The patient was not seen again until April 20, 1933, when she stated that she had been practically free from the disease for several years until a few months before coming back to the clinic. At this date her condition was about the same as it had been in November 1924, except that it was not so severe and the pigmentation was less marked. She was seen irregularly during 1933. On Feb. 13, 1934, a hematologic examination showed: erythrocytes, 3,280,000; leukocytes, 7,150; hemoglobin, 75 per cent;

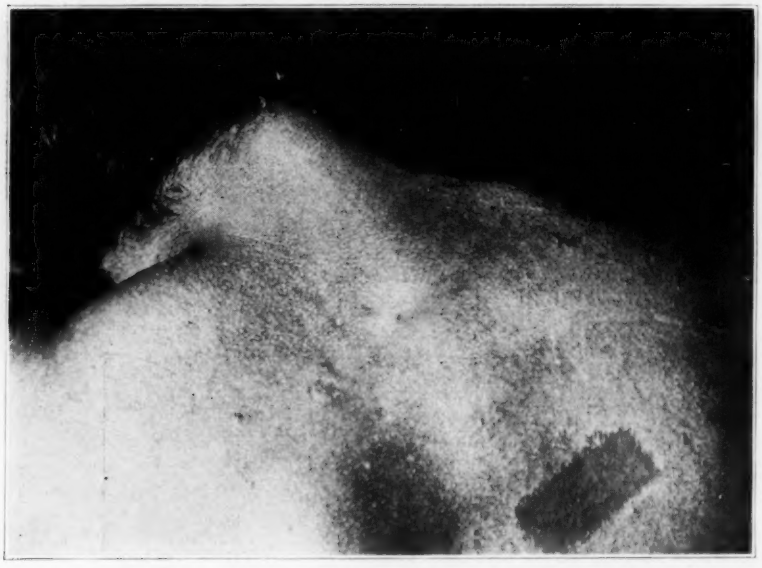

Fig. 3 (case 2).—Photograph showing the remains of lichenoid papules with whitish centers and only moderate pigmentation. The larger lesions are acne vulgaris.

polymorphonuclears, band type, 9.15 per cent, and segmented, 47.5 per cent; small lymphocytes, 28 per cent; large lymphocytes, 0.5 per cent; mononuclears, 4.5 per cent; basophils, 2 per cent; eosinophils, 8 per cent; plasma cells, 1 per cent; anisocytosis, 1+; reticulocytes, less than 0.5 per cent; degenerative index, 8 per cent.

The basal metabolic rate was determined on June 2, 1934. Immediately after the test the patient was given 150 Gm. of protein, two large slices of bread with butter, and a glass of milk. After this meal the basal rate was determined at half-hour intervals for two hours. The results were estimated according to the Harris-Benedict and DuBois methods, and the average was taken. The basal metabolic rates were: —5.8; —13; —20.4; —13.5; and —0.5. From our experiments it seems that if there is no anterior pituitary insufficiency there should be a rise in the basal rate amounting to from 20 to 40 per cent. The test on this patient showed normal thyroid activity and a moderate pituitary insufficiency.

Examination of the patient on Aug. 3, 1934, gave the following results: The lower limbs and the lower part of the trunk were practically normal. The hands were normal, and the skin of the arms was pigmented and somewhat thickened. On the upper parts of the arms there were small lichenoid papules, which were also seen on the upper part of the trunk and the lower part of the neck. In the pigmented areas on the trunk where there were no lichenoid papules and on some of the papules themselves, the follicular openings were white and stood out in marked contrast to the surrounding brownish-black color. The face was still pigmented.

This patient had never received any arsenical medication, but for years she had been using a calamine lotion. Analysis of this lotion showed 0.840 mg. of arsenic per hundred grams of dried substance. The source of the arsenical intoxication in this patient was food contaminated with arsenic plus absorption of the element through the inflamed skin from the use of this lotion.

In 1925, five specimens of urine were examined. The amount of arsenic found varied from 0.04 to 2.49 mg. per hundred grams of dried substance. In 1934, one specimen of blood was examined, which showed 0.04 mg. of arsenic per hundred grams of dried substance. Examination of the hair in 1934 showed 0.059 mg. of arsenic per hundred grams of dried substance and also 11.6 mg. of lead per hundred grams of dried substance.

Case 3.—A. C., a laborer 56 years old, white, born in the United States, was admitted to the outpatient department on Dec. 3, 1930. The duration of the condition of his skin was seven months. The family history and the patient's past history were irrelevant. Examination on admission showed a generalized brownish-black pigmentation, which was most marked on the exposed surfaces. No inflammatory symptoms were present, but there was moderate dental sepsis. For several years he had been working in an oil refining plant, where he handled a clay used in the purification of the oils. After intravenous injections of sodium thiosulphate, an examination of the urine showed 1.11 mg. of arsenic per hundred grams of dried substance. Examination of the hair showed 0.0267 mg. of arsenic per hundred grams of dried substance. The patient drank a large amount of tea, but examination of this showed no arsenic. The clay was examined, and arsenic was found in the following amounts: unburned, 1.19 mg. and burned 1.09 mg., per hundred grams of dried substance.

He showed a steady improvement on eliminative treatment, which is noted from his clinical record:

June 24, 1931: The face had become slightly scaly.

July 20, 1931: The palms showed deep-seated dyshidrosiform vesicles which dried up rapidly, and on July 24 there remained on these parts moderate desquamation and discrete keratoses at the sites of the vesicles.

August 12, 1931: Up to this date the improvement in the patient's condition had been progressive. Since the dental sepsis had been taken care of, the improvement had been more marked.

The patient remained under treatment for several months, and on Jan. 23, 1933, his condition was good.

July 23, 1934: The patient was reexamined and presented only slightly pigmented skin on the face, neck, arms and chest; the forearms, hands and shoulders were moderately pigmented. Over the spinal column there was a deeply pigmented area. The groins were moderately pigmented, the genitals slightly more so, and the palms and the lower limbs were normal. All of the pigmented areas showed white spots at the follicular openings. These white points were not present on admission.

Between Dec. 3, 1930, and June 27, 1932, eleven chemical examinations of the blood were made. The chloride content varied from 450.1 to 499.1 mg. per hundred cubic centimeters, the sugar from 89.4 to 111.2 mg. and the urea nitrogen from 13.8 to 24.6 mg.; the uric acid averaged 3.5 mg.; the carbon dioxide content was normal.

CASE 4.—S. R., a 38 year old man, a Polish Jew, first seen on Jan. 20, 1930, gave the following history: In September 1927, an eruption appeared on the dorsa of his hands, which was intensely pruritic and spread to the forearms and upper

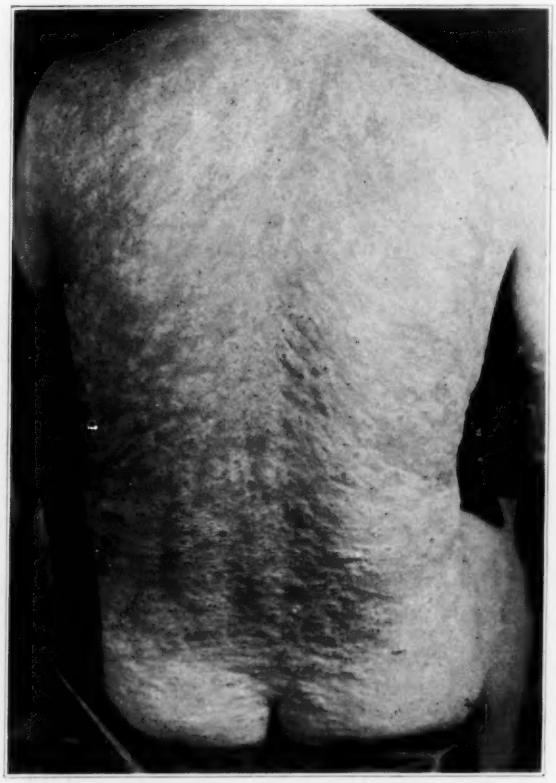

Fig. 4 (case 4).—View of back showing the edema of the skin, the pigmentation, the crusting and the granulomatous lesions.

parts of the arms. He was seen by a dermatologist, who diagnosed the condition as eczema. Soon after this, furuncles developed in the groins and on the scrotum. A second physician gave him injections of arsphenamine and external treatment. During this therapy his face and trunk became involved. A third physician gave him injections of a colloidal silver preparation. Following these injections a high temperature persisted for three weeks and an exacerbation of the cutaneous disturbance. He then went to another physician, who gave him injections of sodium thiosulphate.

He next went to Europe and was treated in Hamburg with a strong keratolytic ointment, which he claimed caused a complete clearing up of the skin but left a

dark color. A few days after his coming back to the United States, the lesions of the skin returned. He went to the Presbyterian hospital and shortly afterward was referred to my service. During his stay of two months in the Presbyterian Hospital the condition became progressively worse. On admission to the hospital he showed a universal exfoliative dermatitis with edema and oozing. His whole body was intensely pigmented. Physical examination showed only dental sepsis. During his stay in the hospital his temperature was slightly below normal in the early morning. At other times it was normal. The blood count on admission was: red cells, 3,860,000; white cells, 6,400. The differential white cell count showed: polymorphonuclears, 68 per cent; lymphocytes, 31 per cent; basophils, 1 per cent. He was discharged on June 14, 1930, showing improvement. After his discharge from the hospital he was treated in the outpatient department. The following notes are from his clinical history:

August 11, 1930: The inflammatory condition had disappeared entirely and only pigmentation was left.

Sept. 17, 1930: The pigmentation was less marked but a dermatitis had appeared on the legs.

Nov. 22, 1930: The perifollicular lichenoid papules which had been present on the trunk and limbs were not so marked. The pruritus was less severe.

A urinary proteose (after the method of Barber and Oriel) was prepared and added to the treatment. Injections of it were given intradermally three times a week. These injections were discontinued after a month, as they seemed to have no effect.

Dec. 24, 1930: During the past few months granulomatous lesions (similar to those seen in case 1) had developed over the entire body.

The patient was readmitted to the hospital on Dec. 24, 1932, with the condition about the same as when he was first seen. A biopsy on Feb. 6, 1931, gave the following results: There was apparently normal epidermis covered by slight parakeratotic scales. Around the dilated blood vessels in the corium there was moderate edema. Large quantities of brown pigment were present. A diagnosis of dermatitis was made.

After his second admission to the hospital, the differential blood count on Dec. 24, 1932, was: hemoglobin, 79 per cent; red cells, 3,660,000; white cells, 12,400; polymorphonuclears, 61 per cent; lymphocytes, 27 per cent; eosinophils, 12 per cent; transitionals, 0.0. On Jan. 11, 1933, the blood count showed: hemoglobin, 79 per cent; red cells, 4,280,000; white cells, 5,800; polymorphonuclears, 53 per cent; lymphocytes, 25 per cent; eosinophils, 20 per cent; transitionals, 2 per cent.

During the period of observation of this patient, twenty-three specimens of blood were examined. The chloride content varied from 412.1 to 528.3 mg. per hundred cubic centimeters; the sugar from 84.2 to 120.8 mg., and the urea nitrogen from 7.5 to 22.8 mg.; the uric acid content was normal. The calcium content varied from 8.9 to 10.8 mg. and the phosphorus from 3.2 to 4.2 mg. The product of the calcium by the phosphorus was, however, within normal limits. The carbon dioxide, expressed in volumes per cent, varied from 64.9 to 69.

The results of three examinations of the urine for arsenic varied from 0.048 to 0.151 mg. per hundred grams of dried substance. One examination of the urine for lead showed 0.23 mg. per liter. A specimen of skin showed 1.018 mg. of arsenic per hundred grams of dried substance. The patient was discharged on Jan. 20, 1933, slightly improved.

In this case there were present the same follicular papules, the same universal pigmentation and the same granulomatous lesions as were seen in cases 1 and 2. In view of the intense pigmentation an examination of urine was made for melanin, and 405.1 mg. was found in 1,650 cc. of urine. There was a definite history of arsenical medication.

Case 5.—B. S., a 34 year old man, Jewish, was referred to one of us (T.) on Dec. 10, 1932, by Dr. William H. Best, of Brooklyn. He was occupied at that time as a draftsman, but for many years he had worked in a brass foundry. He denied having taken any arsenical medication. His cutaneous disorder had begun six years previous to admission and had been generalized for ten months. Examination showed generalized pigmentation and excoriated, thickened plaques on the trunk and the limbs. The whole skin was covered with the same follicular lichenoid papulovesicles, but there was very little exudation. The thickened plaques were the same as the granulomatous lesions seen in the aforementioned cases. A clinical diagnosis of lichen planus had been made before admission. The routine examination of the urine gave normal results, as did the physical examination. The blood count showed: hemoglobin, 84 per cent; red cells, 5,530,000; white cells, 10,400. The differential count showed: polymorphonuclears, 48 per cent; lymphocytes, 37 per cent; eosinophils, 15 per cent; transitionals, none.

Two pieces of skin were removed for histologic study, one from the right side and one from the right arm. The skin from the side showed: epidermis with well marked, more or less regular, rete pegs with some clubbing at the bases; thin suprapapillary plates; a slight amount of edema in parts of the epidermis; marked edema of the papillary bodies; blood vessels of the corium not engorged but surrounded by cellular exudate with a moderately brown pigment in places. The skin from the arm showed: a very irregular epidermis with well marked rete pegs; the basal cell layer not distorted; dense infiltration about the blood vessels in the upper portion of the corium; some pigmentation of the corium; areas of connective tissue, which took a basophilic stain, and practical absence of scales. The pathologic diagnosis was eczema.

The patient was discharged to the outpatient department on Jan. 7, 1933, in an improved condition. He was treated in this department until March 28, at which time he was sent to the hospital again for exacerbation of the cutaneous condition. He remained in the hospital only a short time. The skin then became thickened, scaly and intensely pigmented, and the granulomatous lesions began to look like those in mycosis fungoides. In addition to the hematologic examination on admission another was made on March 30, 1933, and showed: hemoglobin, 80 per cent; red cells, 4,970,000; white cells, 15,400. The differential white cell count showed: polymorphonuclears, 60 per cent; lymphocytes, 25 per cent; eosinophils, 15 per cent. A piece of excised skin was examined for arsenic and showed the enormous amount of 4.5 mg. per hundred grams of dried substance. The urine before the administration of sodium thiosulphate was negative for arsenic. After its administration the urine showed 0.096 mg. per hundred grams of dried substance. Lead was not found. Three chemical examinations of the blood were made. The chloride content varied from 454.3 to 491 mg. per hundred cubic centimeters; the sugar from 76.2 to 96 mg. and the urea nitrogen from 12.9 to 14.4 mg.; the uric acid content was normal. The carbon dioxide content, expressed in volumes per cent, varied from 58.7 to 68. After leaving the hospital the patient went to a private physician, who treated him with keratolytic ointments for several months. A letter from the patient dated Aug. 28, 1934, stated that he had entirely recovered. This was confirmed by his physician, Dr. D. I. Solomon.

COMMENT

Five cases have been described, in each of which there were symptoms not seen in the cases that one encounters in ordinary private or dispensary practice. In four there were lesions of the skin, which, to our knowledge, have not been described before. The patient in case 3 presented typical pigmentation (the whole surface of the body was almost black). The white points at the openings of the hair follicles were not present until he had been under treatment for several months.

Crocker (1903)[2] stated that in the beginning of the pigmentation the hair follicles are absent and they stand out like white points but that as time goes on the pigmentation becomes uniform. In early stages this lack of pigmentation of the follicles is probably due to the fact that arsenic is eliminated partly through the hair follicles, but later their eliminative power is overwhelmed and the metal is deposited there as well as in the surrounding skin.

A dyshidrosiform eruption on the palms such as that present in case 3 is extremely rare, and we have seen only two patients with it, this man and another patient to whom injections of a preparation of colloidal gold had been given for a supposed gastric malignant process. However, hyperhidrosis of the palms in arsenical intoxication is well known. These palmar vesicles represent the starting points of the keratoses seen in conditions resulting from metallic absorption. If treatment is started while they are present, keratoses do not develop. The development of these vesicles while the patient was under treatment seems to have been caused by the liberation of some of the stored arsenic by the administration of sodium thiosulphate. The appearance of the white points in cases 2 and 3 while the patient was under treatment shows definitely that the retained metal had been removed from these parts before it was taken from the surrounding skin. By this we do not mean to say that all the pigmentation is directly due to retained arsenic. It is chiefly due to melanin. How arsenic stimulates the increased formation is not clear. It may be by stimulating the formation or action of the dopa-oxidase, which, acting on the dioxyphenylalanine and brought to the skin in increased amounts in the inflammatory hyperemia, causes increased formation of melanin and, in all probability, represents a protective process.

The condition of the skin in the other four cases was unique. We have not seen it in any other cases. The photograph (close-up) of the patient in case 1 shows clearly the peculiar follicular lichenoid lesions. In acutely inflamed stages these lesions show minute vesicles at their apexes and may show serous exudation. In stages of quiescence, the

2. Crocker, R.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1903, p. 474.

vesicles are not present and the follicular lesions are hard. The acuminate papules are about the size of the head of a pin and are deeply pigmented, disappearing before the absorption of the follicular infiltration. The granulomatous lesions are of varying sizes from ¼ to ¾ inch (0.6 to 1.9 cm.) in diameter. They are elevated about ¼ inch (0.6 cm.). The skin over them is pigmented and may or may not show the follicular papules. They are moderately firm to the touch but are never indurated as much as lesions seen in mycosis fungoides. Their histologic appearance in the early stages is that of simple inflammation. Later in the course of the process the histologic picture represents that of chronic granuloma (case 1). The fact, however, that the patient in case 1 recovered, that the patient in case 2 is free from symptoms suggestive of lymphogranulomatosis and that the patient in case 5 has entirely recovered is very much against the supposition that this type of eruption may be premycotic.

Aschoff (1924)[3] stated in his lecture on the reticulo-endothelial system: "It is well known that the histiocytic system and the apparently closely related hematopoietic system can be so greatly stimulated, particularly by metals in colloidal solution, that leukemic-like proliferations can be experimentally produced in this manner."

In another case of arsenical dermatitis observed but not included in this report, a lymph node showed a structure suggestive of pseudoleukemia which is steadily improving. In this case the examination of the urine after treatment with sodium thiosulphate showed 0.040 mg. of arsenic. The blood contained 0.06 mg. of arsenic; the scales of the skin, 4.380 mg., and the hair, 0.455 mg. These determinations are based on the amount found in 100 Gm. of dried substance. The clinical condition was a generalized exfoliative dermatitis with adenopathy of the cervical and inguinal nodes.

Hematology.—Studies of the blood were made on the four patients presenting the peculiar lichenoid and granulomatous lesions. Each had secondary anemia of varying intensity. On one patient (case 5) at the first examination a relative lymphocytosis was seen, but this had disappeared by the second examination. The eosinophils showed an increase with each count. We do not think that this was of much importance, as eosinophilia is seen frequently in many dermatologic conditions. Examination of another patient (case 1) showed 7 per cent myelocytes. This in all probability was due to the action of the arsenic on the bone marrow and, as Aschoff said, caused conditions resembling leukemia. Clough (1929)[4] stated that myelocytosis can be seen in severe infec-

3. Aschoff, L.: Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924, p. 32.

4. Clough, Paul W.: Diseases of the Blood, Harper's Medical Monographs, New York, Harper & Brothers, 1929, p. 70.

tions with functional injury to the bone marrow and in intoxications of various sorts similarly injuring the bone marrow. That it was not a true myelogenous leukemia is probably shown by the fact that this examination was made in March 1927 and a letter received in October 1929 stated that the patient was almost well.

Histologic Studies.—These were made on four patients, i. e., on those showing granulomatous and lichenoid lesions. In each case there was nothing found which could not be interpreted as chronic inflammation. Three of the examinations were made in our service and one at the Montefiore Hospital. The pathologist at that hospital diagnosed the condition as chronic granuloma of the skin.

Ullmann (1930) [5] stated that 1 part of arsenic in 40,000,000 added to embryonal cells acts on them in a tumor-forming manner, and, accordingly, in small amounts it acts on many tissues and types of cells. This cellular change and proliferation are seen especially at the follicles and are a reaction of the cells of the hair sheaths and of walls of the follicles due to elimination of the metal through the sebaceous and sweat glands. In some cases this cellular metaplasia assumes a malignant character and, as is well known, carcinoma develops.

Therefore, it may be reasoned that arsenic can cause a lymphogranulomatous condition. Whether this occurs is impossible for us to say. We have not been able to observe a case of this type for a sufficiently long time without treatment.

Blood Chemistry.—Repeated chemical examinations of the blood were made in cases 3, 4 and 5. These examinations included tests for chlorides (Whitehorn method), sugar (Hastings-Maclean method), urea nitrogen, uric acid, carbon dioxide content in volumes per cent (Van Slyke method), calcium and phosphorus. There were no changes in the calcium-phosphorus ratio, and the amount of uric acid was practically always normal. The carbon dioxide content in volumes per cent was normal in cases 4 and 5. In case 3, however, it varied from 64.9 to 69. This rise in the carbon dioxide content we have frequently seen in other cases of arsenic retention in which the patients were treated with sodium thiosulphate. In all probability, such an increase in carbon dioxide is due to the arsenic, and it seems to be a symptom of alkalosis, although it is well known that a diagnosis of alkalosis cannot be made from a simple determination of the carbon dioxide content alone. We believe that when it rises above 65 volumes per cent sodium thiosulphate is contraindicated and a calcium preparation should be submitted for it.

There was a wide variation in the content of sugar and chlorides in the blood. The normal amount of sugar, according to the method used, is from 90 to 96 mg. per hundred cubic centimeters of blood,

5. Ullmann, K.: Tr. Internat. Cong. Dermat. & Syph., 1930, p. 693.

and the normal chloride content is from 440 to 460 mg. In case 3 the sugar content varied from 84 to 120 and the chlorides from 412.1 to 528.3 mg. In case 4 the sugar varied from 89.4 to 111.2 and the chlorides from 450.1 to 499.1 mg. In case 5 the sugar varied from 76.4 to 96.2 and the chlorides from 454.3 to 491.9 mg. In case 3 carbon dioxide was found at one time to be 69 volumes per cent.

Increase in the chloride content of the blood during treatment with sodium thiosulphate occurs frequently and seems to be an endeavor on the part of the body to prevent alkalosis from developing. The chloride ion is drawn from the red cells to neutralize the excess of sodium bicarbonate formed by the action of the sodium thiosulphate.

The amount of urea nitrogen in case 3 was within normal limits. In this case the chief symptom was pigmentation. In cases 3 and 5, however, the amount of urea nitrogen showed wide variations, being as low as 10.3 mg. in case 3 and 12.9 mg. in case 5. The decrease in this substance, we believe, indicates a lowered hepatic function, although it is stated that the amount of urea nitrogen in the blood cannot be taken as a criterion of activity of the liver.

Normal Arsenic Content.—Before discussing the chemical findings in these cases, it is necessary to state the amounts of arsenic in the tissues and fluids of the body which may be considered normal, and although we believe that any amount is abnormal it must be admitted that there are persons in whom no abnormalities can be found who show arsenic in their blood and urine.

Heller (1927)[6] quoted Billeter and Marfut who found the following averages (expressed in milligrams per hundred grams of tissue and per liter of fluids) in the corpses of fourteen persons to whom arsenic had not been administered in the form of medication.

Nails	—0.0172	Heart muscle	—0.0104
Thyroid	—0.0131	Urine	—0.0104
Brain	—0.0111	Skin	—0.0097
Bone	—0.0825	Liver	—0.0111
Hair	—0.0097	Blood	—0.0083
Spleen	—0.00875	Lungs	—0.0095

Oppenheim (1931)[7] claimed that the normal amount in the scales of the skin was 0.0026 mg. per hundred grams of tissue and in the urine, 0.0005 mg. per liter of fluid.

We have considered the amount in the urine below which we have been unable to demonstrate any clinical symptoms as 0.03 mg. per hundred grams of dried substance. By knowing the specific gravity and the total solids this can easily be converted into the amount per liter.

6. Heller, S., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 13, pt. 2, p. 31.

7. Oppenheim, M.: Dermat. Wchnschr. **92**:741 (May 16) 1931.

Diagnostic Procedure.—For any metal to exert a pathologic action it must be retained in some part of the body, and the mere finding of it in the urine or the blood may mean absolutely nothing. Our procedure is as follows:

Specimens of blood and urine are examined and the amounts of arsenic present noted. There may be none, or a small amount may be found. An intravenous injection of 10 cc. of a freshly prepared 10 per cent solution of sodium thiosulphate is given, and the urine is collected for twenty-four hours and examined for arsenic. If arsenic is found in these second specimens when none was found in the first, or if the amount found in the first examination is materially increased and is more than 0.03 mg., the amount is pathologic and has some causal relationship to the clinical condition. The reason for this increase after the administration of sodium thiosulphate is that arsenic has been deposited in the tissues in combination with protein in the form of a colloidal arsenous sulphide having combined with the sulphydryl radical of glutathione and that of cysteine. This compound is insoluble in the blood and body fluids, but it is soluble in solutions containing sulphydryl radicals.

Results of the chemical examinations in the aforementioned cases shows that the skin was examined on the patients in cases 4 and 5. In case 4 the amount of arsenic found was 1.018 mg. per hundred grams of dried substance, or more than 100 times the normal amount. In case 5 the amount was 4.5 mg., or more than 450 times the normal amount. In case 2 the amount found in the hair was 0.059 mg. per hundred grams of dried substance. In case 3 it was 0.267 mg. In both cases the amount exceeded the normal many times.

Reference to the results of the urinalyses shows in all cases the presence of arsenic in very greatly increased amounts. These amounts vary from time to time from none to 2.63 mg. As we have reported previously (1926),[8] the elimination of the retained arsenic is not uniform, there being periods of ebb and flow. This retention at times is in all probability due to a temporary change in the acid-base balance of the blood. In conditions in which alkalosis is present sodium thiosulphate does not act. This we have found a great number of times, and Spillmann, Vérain and Weis (1932)[9] also stated that sodium thiosulphate is inactive in states of alkalosis.

Treatment.—The use of sodium thiosulphate for the treatment of metallic intoxications is so well known that a discussion of its value seems to be superfluous. There are, however, some points which we think it advisable to bring out.

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8. Throne, B.; Van Dyck, L.; Marples, E., and Myers, C. N.: Arsenic as an Etiological Factor in the Genesis of Eczema, New York State J. Med. **26**:843 (Oct. 15) 1926.

9. Spillmann, L.; Vérain, M., and Weis, J.: Le p_H en dermatologie, Paris, Masson & Cie, 1932.

The arsenical dermatoses caused by inorganic arsenic are much more difficult to influence than are those caused by organic arsenic or arsphenamine. In the first instance the arsenic has been completely oxidized, or nearly so, while in the second it exists in a trivalent form. This means that its combination with the tissues is more stable and more difficult to break up, and necessarily treatment must be of much longer duration.

The form in which sodium thiosulphate is used is of most importance. Prepared solutions which are on the market are of no value. We have tried and discarded them. The compound is very unstable when in solution, and therefore only solutions freshly prepared at the time of administration should be used. The dose is from 0.5 to 1 Gm. in a 10 per cent solution, given every third day. Enterically coated tablets (0.5 Gm.) can be given on the other days, i. e., one tablet before meals. This method of treatment must be continued for months. It is necessary to watch for the development of alkalosis. If possible, chemical examinations of the blood should be made at intervals of about two weeks. When this is not feasible, the following clinical symptoms show a contraindication to sodium thiosulphate: (1) an exacerbation of the cutaneous symptoms as shown by increased edema of the skin; (2) exacerbation of the serous exudation; (3) increased subjective symptoms; (4) pruritus (especially), and (5) lowered blood pressure and a feeling of languor.

When these symptoms appear we have found the administration of a calcium preparation of value. We prefer calcium chloride carbamide (afenil). Tests for toxicity which we have made with this preparation show it to be only one-sixth as toxic as ordinary calcium chloride.

If chemical examinations of the blood can be made, a carbon dioxide content of over 65 volumes per cent calls for the substitution of the calcium preparation or for a decrease in the amount of the thiosulphate given. A chloride content in the blood of over 500 mg. is an absolute contraindication for thiosulphate.

In acute cases, in which there is a marked decrease in the urea nitrogen of the blood, sodium thiosulphate can be given in solution of dextrose. Fairly large amounts of dextrose can be given by mouth together with 1 unit of insulin for each 3 to 5 Gm. of dextrose.

We have not tried giving ammonium chloride together with the thiosulphate to prevent the development of alkalosis. It might be of value. Locally, keratolytic ointments seem to be of value in hastening the elimination of the arsenic contained in the skin.

In view of the constant exposure to arsenic from food and occupation, it is evident that persons who once have shown evidence of its retention should receive eliminative treatment at intervals of six months or so.

In regard to the general treatment, it is needless to state that any abnormality found should be corrected. We do not know the reasons why some of those exposed retain the element and others eliminate it. Previous cellular damage is the probable explanation, and in many patients whom we have seen and treated this cellular damage seems to have been caused by focal infection; at least the removal of the infected foci was followed by a more marked and rapid improvement, and in some patients improvement was not seen until after the removal of infected teeth or tonsils.

In case 4 the finding of 405.1 mg. of melanin in 1,650 cc. of urine, or 245.5 mg. per liter, seems to be definite proof of the enormous increase in the formation of melanin. Further than this we can say nothing. Peters and Van Slyke (1931)[10] stated that with the exception of a case of acute hepatic cirrhosis, they never were able to demonstrate the presence of melanin in the urine except in cases of melanotic sarcoma. We regret that similar examinations were not made in our other four cases.

SUMMARY

Five cases of marked retention of arsenic together with the laboratory findings have been reported. Four of these patients presented extremely peculiar lesions of the skin. In all patients an extremely large amount of arsenic was found. We believe that the retention of arsenic was the chief cause of the manifestations presented. The treatment of conditions due to arsenic has been discussed.

We do not know the significance of the melaninuria found in case 4. It may be possible that conditions of this type, if not treated by eliminative measures, may undergo a transition to some form of lymphogranulomatosis. This may happen also to patients who have received such treatment. Arsenical medication may cause this condition, but occupational contacts and contamination of food with arsenic also may do it.

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10. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry: Interpretations, Baltimore, Williams & Wilkins Company, 1931, vol. 1, p. 1166.

LYMPHOGRANULOMA INGUINALE

REPORT OF A CASE WITH INVOLVEMENT OF RETROPERITONEAL LYMPH NODES AND PROBABLE INVOLVEMENT OF THE HIP JOINT, ADRENALS AND KIDNEYS, WITH AUTOPSY

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It is generally assumed that the lesions of lymphogranuloma inguinale are limited to those of primary infection and local bubo.[1] There are many observations on record,[2] however, of fever, rigors, malaise, weakness, loss of weight and such rheumatoid manifestations as erythema nodosum, episcleritis, periarticular pains and polyarthritis, and some authors have therefore suggested that the disease may at times spread beyond the local lymphatic barrier. Frauchiger[3] recently described two cases of anorectal syndrome with a positive Frei reaction, which exhibited chronic polyarthritis affecting the elbows, knees and wrists. The arthritic manifestations of one patient improved on resection of the rectum. In the other a para-articular abscess was discovered, which proved to be sterile by ordinary methods of bacteriologic examination.

From the Department of Pathology and the Department of Dermatology and Syphilology of the Medical Department of the Western Reserve University and of the Cleveland City Hospital.

1. Maresch, R., and Chiari, H., in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1931, vol. 6, pt. 3, p. 320. (Literature to and including 1929.) Fischl F., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 21, p. 364.

2. Cole, H. N.: Lymphogranuloma Inguinale, the Fourth Venereal Disease, J. A. M. A. **101**:1069 (Sept. 30) 1933. Levaditi, C.; Ravaut, P., and Cachera, R.: Les preuves de la nature lymphogranulomateuse de la maladie expérimentale du singe, Bull. Soc. franç. de dermat. et syph. **38**:1456, 1931. (Cited from Stannus, H. S.: A Sixth Venereal Disease, London, Ballière, Tindall and Cox, 1933.) Finlay, G. M.: Experiments on the Transmission of the Virus of Climatic Bubo to Man, Tr. Roy. Soc. Trop. Med. & Hyg. **27**:35, 1933. (Cited from Stannus.) Levaditi, C.; Marie, A., and Lépine, P.: Conservation du virus lymphogranulomateux, Compt. rend. Soc. de biol. **107**:1496, 1931. (Cited from Stannus.) DeWolf, H. F., and Van Cleve, J. V.: Lymphogranuloma Inguinale, J. A. M. A. **99**:1065 (Sept. 24) 1932.

3. Frauchiger, E.: Polyarthritis lymphogranulomatosa inguinalis tarda, Schweiz. med. Wchnschr. **63**:1207, 1933.

Whether these phenomena are produced by the virus or are merely expressions of sensitization to a foreign protein is yet uncertain. The fact that the virus of lymphogranuloma inguinale causes encephalitis in monkeys and when carried back to man again gives rise to the characteristic inguinal adenopathy may be taken as evidence that the infecting agent can attack more than one type of tissue. In the literature little attention has been given to the extralymphatic localizations of the disease. This can probably be accounted for by the fact that lymphadenopathy is the predominant feature, that any involvement of the other viscera usually does not produce clinical manifestations and that detailed postmortem study has in the past been infrequent because the patient rarely dies of this ailment. We have been able to find reports of only two cases with autopsies [4] since this disease was first discovered in 1859.[5] In both cases nothing further was revealed than what had already been learned of the disease by means of examination of specimens removed for biopsy and at operation. We therefore present the following case of lymphogranuloma inguinale in a patient who, after having been observed for four and one-half months before death, came to autopsy. The results of the postmortem examination deserve especial consideration.

REPORT OF CASE

History.—W. B., a Negro, aged 31, was admitted to the hospital on Jan. 12, 1932. Two months previously he had had a urethral discharge lasting fifteen days. Three weeks after the cessation of this discharge a swelling in the right inguinal region developed, which progressed to spontaneous rupture before he came to the hospital. When first seen, the right inguinal region contained several large nodes fused into a single mass; the skin was deeply pigmented and adherent, and there were several discharging sinuses. The left inguinal region was tender, but the nodes were only slightly enlarged. There was neither a penile sore nor a urethral discharge at this time. The pain in the groin interfered with his normal gait and was especially severe on extension of the right thigh.

The Frei reaction was strongly positive; tuberculin reactions were negative in dilutions of 1:1,000,000 and 1:100,000. A series of fourteen Wassermann reactions of the blood varied from negative to three plus, all those reported later being negative. Except for an occasional cast or leukocyte and traces of albumin, urinalyses gave negative results. The initial blood count showed 4,520,000 erythrocytes and 9,200 leukocytes with 78 per cent polymorphonuclears.

4. Hillsman, J. A.; Wilshusen, H. F., and Zimmerman, H. M.: Lymphogranulomatosis Inguinalis: Report of a Case of Twenty Months' Duration with Autopsy Observations, Arch. Dermat. & Syph. **18**:383 (Sept.) 1928. Wernich: Ueber Poradenolymphitis oder Lymphogranulomatosis inguinalis subacuta Nicolas-Favre, Przegl. Dermat., 1926, vol. 21. (Cited from Zentralbl. f. Haut- u. Geschlechtskr. **24**:137, 1927.)

5. At the time of publication, two additional reports of autopsies on patients with lymphogranuloma inguinale have come to our notice: Wien, M. S., and Perlstein, M. O.: M. Rec. **139**:288, 1934, and Wien, M. S.; Perlstein, M. O., and Neiman, B. H.: Arch. Path. **19**:331 (March) 1935.

Ten intravenous injections of typhoid vaccine were given at biweekly intervals, and four intravenous injections of a 1 per cent solution of antimony and potassium tartrate totaling 18 cc. were given at similar intervals, without result. Meanwhile several new areas of fluctuation had developed and ruptured to form new sinuses. In view of this poor response to chemotherapy, complete resection of the right inguinal lymph nodes was done on March 17, four months after the onset. Pain on extension of the right thigh was again observed at the time of operation but was ascribed to the bubo. After the operation the temperature rose to 40 C. (104 F.), where it remained for several days before showing an intermittent character, ranging from 37 to 39.5 C. (98.6 to 103.1 F.). Because of the marked febrile reaction and continued pain in the right hip, a roentgenogram of the joint was taken a week after the operation, which, however, revealed no lesion. The upper end of the surgical wound soon broke down and began to discharge pus in increasing amounts. The septic fever persisted, and the general condition became progressively worse. The leukocyte count now varied from 14,300 to 17,000, and occasional showers of casts, pus cells and traces of albumin were present in the urine. A second roentgenogram of the pelvis taken one month after the first showed a definite destructive process in the right hip joint. On the following day, April 23, arthrotomy was performed, releasing a large amount of pus and exposing eroded articular cartilages. Drains were inserted and extension applied to the leg but the pain, sepsis and debility grew progressively worse, and the patient died on May 30, six and one-half months after the onset.

The autopsy was done by Dr. W. W. Corwin fourteen hours after death.

Gross Observations.—External Appearance: There was a fairly recent operative incision located above and posterior to the right inguinal ligament. The lower portion of this incision was still open. There was another fairly recent incision directly below and at right angles to the upper incision. The upper and central portions of this incision were open, and there was a sinus extending down to the soft tissues and into the right hip joint. A few small, discrete nodes were palpated in the left inguinal region.

Thorax: The left lung was diffusely adherent to the wall of the chest by fibrous adhesions. Except for anthracosis, there were no gross changes of note in the lungs. The heart showed no gross changes of importance.

Abdominal Cavity: There were many adhesions between the omentum, abdominal wall, colon, gallbladder, appendix and surrounding tissues. There was no free fluid.

Gastro-Intestinal Tract: There was a large and typical peptic ulcer at the lesser curvature about 7 cm. from the pyloric orifice. Aside from this the gastrointestinal tract showed nothing of note.

Spleen: The spleen weighed 75 Gm. It cut with moderate resistance, and the cut surface was light red and smooth. Trabeculations were prominent, and malpighian corpuscles were indistinct.

Liver: The liver weighed 1,150 Gm. It cut with ease, and the cut surface was smooth and brown. The gallbladder contained a small amount of bile. The bile ducts were patent.

Pancreas: The pancreas showed no changes of note.

Adrenals: The left adrenal was markedly increased in size. It was somewhat adherent to the upper pole of the kidney. The capsule was thickened. On section the cut surface was dark red and apparently hemorrhagic. A few small, yellow areas measuring from 2 to 3 mm. were seen. The right adrenal was also firmly adherent to the kidney. The cortex appeared as a thin, yellow rim of tissue, whereas the remaining portion of the adrenal was a soft, red and apparently hemorrhagic mass.

Kidneys: The left organ weighed 150 Gm. The capsule stripped with ease. The cortex measured 6 mm. Three yellow, nodular masses measuring at the most 4 mm. in diameter were present at the transitional zone between the cortex and medulla. The same type of lesions (although smaller) were seen on the surface of the kidney. The right organ weighed 200 Gm. The cortex measured 7 mm. Here, too, an occasional small, slightly elevated, yellow nodule measuring at the most 1 mm. in diameter was present on the surface. Both renal pelves and ureters appeared grossly normal.

Pelvic Organs: The bladder contained about 200 cc. of clear urine. The mucous membrane was pale. The prostate was small and firm; it cut with moderate resistance, and the cut surface was pale and smooth. The testes and seminal vesicles presented no gross abnormalities.

Retroperitoneal Region: Behind the cecum there was a small sinus which was discharging thick yellow pus. This came from a large abscess which had practically destroyed the entire right psoas muscle and which extended from the cecum to the second lumbar vertebra. The abscess was filled with thick yellow pus and had a dark gray, granular wall with considerable induration of surrounding tissue. Lying ventral to the muscle, particularly in the upper lumbar region, were enlarged retroperitoneal lymph nodes which were, for the most part, discrete. The cut surface was pink and smooth. Others were darker and nodular. In the latter were many yellow follicular areas from which pus could be expressed similar to that in the large abscess. The lymph nodes at the bifurcation of the aorta and along both iliac arteries were also enlarged.

Bones: The spine, beginning at the eleventh dorsal vertebra; the entire pelvis, and the proximal portions of both femurs were removed. The only abnormality was in the right hip joint. On opening the capsule of the joint a small amount of dark fluid was observed. The articular surface of both the acetabulum and the head of the femur was markedly roughened and discolored. The sinus which was described in the right inguinal region was observed to enter the right hip joint. The bone marrow of the femur was light red and of jelly-like consistency.

Organs of the Neck: These showed no abnormalities of note.

Brain and Cord: The weight of the brain was 1,300 Gm. The organs showed no abnormalities of note.

Bacteriology: Smears of material from a lumbar node and the psoas abscess showed gram-positive cocci in chains and clusters, gram-negative bacilli and no acid-fast bacilli. A culture of the heart's blood showed Staphylococcus albus. A culture of material from the psoas abscess showed Bacillus coli and Staph. albus.

Microscopic Observations.—Only the organs showing abnormalities of importance in this case will be described.

Retroperitoneal Lymph Nodes: The changes observed in these nodes were obviously of the same character, although the degree of change differed in the various members of the lumbar chain. All the sections showed hyperplasia which was, in general, diffuse. The individual follicles could no longer be identified. The pulp was filled with cells largely mononuclear. However, members of a polymorphonuclear group and larger cells which were obviously phagocytic were also present. The capsule of these nodes was enormously thickened and consisted of dense, often hyalinized fibrous tissue in which, however, little evidence of inflammation could be observed. In the parenchyma, even with the naked eye, follicular structures could be seen. Microscopic examination of these areas revealed them as roughly circular areas of necrosis. These necrotic areas appeared rather

sharply demarcated from the surrounding hyperplastic pulp, and extending into them in the typical palisade fashion were cells, of both the epithelioid and the mononuclear type (fig. 1). The presence of early fibroblasts with some reticulum formation was seen external to this wall of palisaded cells. In general, these follicles were discrete and did not coalesce. Here and there a node was seen, particularly in the lower part of the chain along the right iliac vessel, in which the entire tissue had been replaced by several follicles the centers of which had emptied into the sinus so as to form the "wasp's nest" type of node already described in the literature on lymphogranuloma inguinale. The pulp about the follicles was preponderantly composed of mononuclear cells, and only a few polymorphonuclears were present, some of which were eosinophils. Plasma cells were

Fig. 1.—Section of a retroperitoneal lymph node showing typical discrete lesions of lymphogranuloma inguinale. Hematoxylin and eosin stain; × 10.

also seen. The chromatic bodies described by Gamna were not observed.[6] Gram and Ziehl-Nielsen stains did not reveal any organisms.

Wall of Psoas Abscess: The section showed a hyperplastic lymph node of the character already described, the capsule of which was fibrotic, extraordinarily thickened and firmly adherent to what was apparently the remnants of a psoas muscle. The muscle fibers, however, had lost their nuclei and were partly displaced by connective tissue. The wall of the abscess was composed of granulation tissue. The cells consisted almost exclusively of fibroblasts and mononuclears, many of which had the appearance of plasma cells. A very few polymorphonuclear cells were seen. Young capillaries were present. Staining for acid-fast organisms

6. Dr. Arthur W. Grace examined these slides and concluded that some basophilic and fewer acidophilic intracytoplasmic bodies were present, and that the latter resembled those he had seen in cases of lymphogranuloma inguinale.

revealed none. The Gram stain showed the presence of large gram-positive bacilli in moderate numbers.

Sinus Leading to Hip Joint: Muscle fibers were present, scattered throughout a mass of fibrous connective tissue. Here and there small foci of mononuclears were seen. The sinus had a thick fibrous wall, the innermost portion of which was covered by granulation tissue in which were observed small spicules of bone. The cells of this membrane were chiefly mononuclears, many of which were plasma cells, although many polymorphonuclears were also present. Fibroblasts and larger mononuclear cells with a vacuolar cytoplasm were seen. Gram stains did not reveal the presence of organisms.

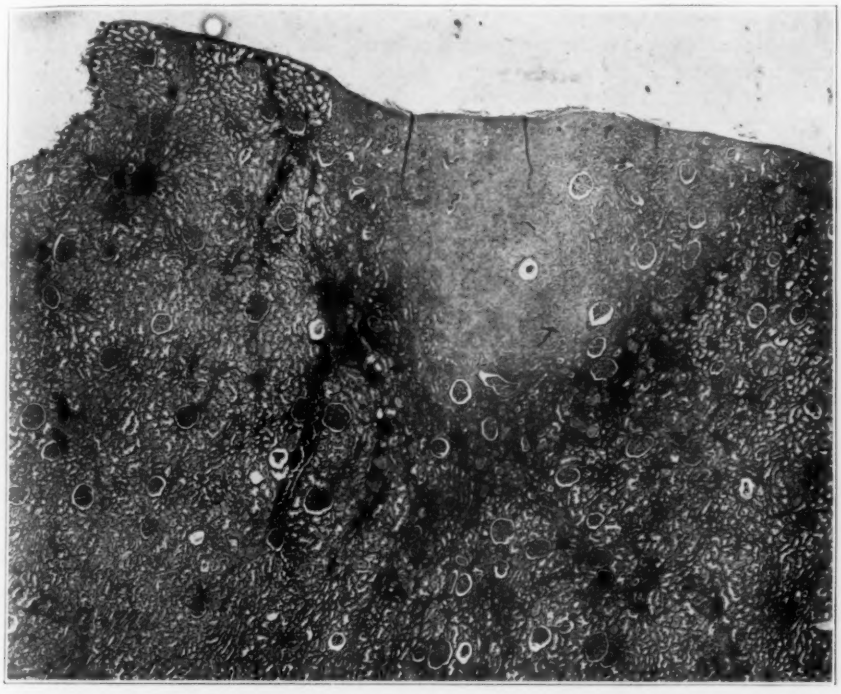

Fig. 2.—Section of a kidney showing a cortical nodule with beginning extension toward the medulla. Hematoxylin and eosin stain; × 10.

Capsule of Hip Joint: The connective tissue was greatly increased in thickness, dense and hyalinized. Granulation tissue was present, infiltrated by cells which were almost exclusively mononuclears and fibroblasts. The Gram stain revealed a very few gram-positive coccoid bodies, which might be gram-positive diplococci.

Bone from Hip Joint: This section was composed of normal bone, and surrounding it there was new bone formation in the periosteum, which showed irregular trabeculae extending out in finger-like projections into the connective tissue. The lacunae containing the cells were large and numerous. The bone did not have the fibrillar structure of normal bone. The periosteum was thickened. No evidence of inflammation was seen. A second section showed an area of bone absorption and trabeculae breaking up into a fibrillar mass in which were a few nuclei, mostly of fibroblasts; no true inflammatory exudate was seen.

Kidney: The branches of the cortical veins were remarkably dilated and contained large amounts of blood. There were apparently no premortem clots. There were considerable loss of staining qualities and desquamation of cells into the tubules; this was generalized and was probably due to postmortem changes. Just beneath the capsule, however, there were areas of cellular infiltration. The cells in question were largely mononuclears of the lymphocytic type, but there was also an increase in connective tissue. The tubules and glomeruli in these areas were still recognizable. In other areas the collection of exudate was so great as to constitute small mononuclear abscesses. All kidney structure in these areas had disappeared (fig. 2). Necrotic cells were often present in circular areas which might originally have been glomeruli or tubules. Linear areas of such infiltration might be traced down toward the pyramids. Such areas were distributed at irregular intervals under the capsule and gave the cut section of the kidney the wavy appearance seen in arteriolar disease. A few fibrous balls and a few retention cysts were seen. The arterioles in general had moderately thickened walls. Gram stains and stains for acid-fast organisms revealed no bacteria.

Adrenal: A section was taken through the adrenal and kidney. The capsule of the kidney was thickened and edematous. Between the capsule of the kidney and the adrenal the connective tissue was diffusely and densely infiltrated by inflammatory exudate. In areas this exudate was so plentiful as to constitute an abscess. Here the cells were largely polymorphonuclear. There were extensive necrosis and hemorrhage. The fat was largely destroyed, and young connective tissue was forming. All these changes were retroperitoneal. The peritoneal surface and even the subperitoneal tissues appeared to be uninvolved. Gram stains and staining for acid-fast organisms revealed no bacteria.

In a section taken through the entire adrenal the architecture of the cortex could still be made out. The cells of the columns were preserved for the most part, although in areas there was vacuolation. In the reticular zone, however, the venous spaces were tremendously dilated and were filled with blood; they practically obliterated the normal architecture. In this zone, as well as in the medulla, there were focal areas of necrosis in which all the cells stained a homogeneous deep blue with the hematoxylin and eosin stain. The large veins in the medulla were filled with a typical premortem clot. At one point beginning organization of this clot could be seen proceeding from the wall of a vessel. The veins in the capsule of the adrenal showed the same condition. Furthermore, there was definite infiltration of their walls and of the connective tissue about them by cells which were in part polymorphonuclears and in part cells with large, clear, vesicular nuclei—probably cells of the reticulo-endothelial system.

SUMMARY OF OBSERVATIONS AT AUTOPSY

The discrete follicular lesions of the lymph nodes throughout the entire retroperitoneal chain and the type of cellular exudate represented the morphologic characteristics of lymphogranuloma inguinale. The wall of the psoas abscess showed nothing further than granulation tissue, which, however, was remarkable in that the exudate was composed more of mononuclear cells than of polymorphonuclears. The close association of this abscess with the lymph nodes suggests that the infection may have taken place by continuity from a diseased node.

The adrenals showed the effects of thrombosis of the veins. These thrombi showed definitely that they had developed before death. They

were in part organized and were apparently merely a part of the thrombosis of the veins throughout the soft tissues in which the adrenals were embedded. Outside the adrenals perivascular mononuclear infiltration of the veins could be seen. The fact that the arteries and veins in local lesions in lymphogranuloma inguinale are almost consistently affected, that infiltrations by perivascular cells are common and that the intima may proliferate and ultimately cause occlusion of the vessels has been emphasized by several authors.[1] The sinus leading to the hip joint and the joint itself showed chronic granulomatous inflammation of indefinite character. It is, however, suggestive that the arthritis occurred near the site of the bubo.

The kidneys showed follicular granulomatous lesions, the exudate of which was largely mononuclear. The infiltration was in part in the glomeruli (the condition being one of proliferative glomerulitis), but in the larger part it was in the interstitium and in places led to the formation of small "lymphatic abscesses." Some of these abscesses extended along and between the tubules, into the pyramids. The picture is not that of embolic nephritis. In this connection it is important to bear in mind that the presence of lymphatic tissue in the kidney is well recognized by pathologists.

CONCLUSIONS

This patient appears to have had typical lymphogranuloma inguinale, but in the course of the disease arthritis of the hip and constitutional disturbances developed. The autopsy revealed the typical lesions of lymphogranuloma inguinale in the entire lymphatic chain extending from the inguinal region along the retroperitoneal lymph nodes to the diaphragm. In addition, granulomatous lesions of the kidneys, hemorrhagic infarction of both adrenals, a psoas abscess and chronic arthritis of the hip joint were observed. It appears certain that the disease had in this instance invaded the lymphatic apparatus beyond the local inguinal nodes. The extralymphatic lesions, however, cannot be explained by the information at our disposal. Their histology is not typical of any disease known to us. Tuberculosis can be ruled out not only because of the absence of any acid-fast organisms but also because of the character of the inflammatory granulation tissue. The latter, moreover, did not show the characteristics of a pyogenic infection; the organisms observed by smear at autopsy and in the tissues might well have been due to postmortem invasion. We therefore present this case to stimulate interest in a more complete study of lymphogranuloma inguinale and suggest that in the future tissue be taken from any extralymphatic lesions and tested on susceptible animals.

TREATMENT OF PARAFFINOMA

REPORT OF A CASE

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PITTSBURGH

"Beauty experts" have claimed good results from giving injections of paraffin oil (liquid petrolatum) intradermally to remove blemishes, such as dimples and wrinkles. It is only when there is an untoward result that aid is sought from the dermatologist. Some surgeons claim to get excellent results from giving an injection of liquid paraffin, heated to 40 F., to change the contour of a disfigurement or to treat hernia. The method has been used in removing Bartholin's gland,[1] by first injecting paraffin oil into the cavity to outline it and then excising the gland. There is less tendency for defects to develop when the paraffin is injected into fatty tissue or less vascularized areas. Nevertheless, the patient is never assured that a defect will not occur as a result of this procedure. The deformity may develop in from six months to five years. The technic of giving such injections requires that the paraffin be sufficiently warm and fluid so that uneven hardened areas are not produced.

REPORT OF CASE

Mrs. L., aged 54, on presenting herself on Feb. 20, 1934, had two large masses beneath the lower eyelids. In March 1930, on account of large "bags" beneath the lower eyelids, she consulted a "beauty specialist," who promised a permanent cure and injected a warmed white oil. Ecchymosis and redness, which developed incident to the injection, disappeared within a month. Very soon afterward the patient noticed that the areas felt hard and the masses gradually developed and became larger. When the patient came for consultation, a yellowish-white mass was evident beneath each eye. Slight telangiectasia was noted over the right, and larger, mass only.

The right mass was triangular in outline, with the apex pointing toward the epidermis. The base was irregular, measuring 1¾ inches (4.45 cm.) by 1⅛ inches (2.86 cm.) and extending toward the nasal area. It was attached rather firmly to the subcutaneous tissue and to the orbital and nasal areas of the maxilla. The mass could be outlined definitely, and it seemed as if it could be easily shelled out.

After injecting infra-orbitally a solution of 2 per cent procaine hydrochloride and epinephrine for anesthesia, I incised and separated the epidermis and dissected out the fibrotic tissue. The mass was not encapsuled, and fibrotic finger-like

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From the Pittsburgh Skin and Cancer Foundation.

1. Auster, Lionel S.: Technique of Excision Following Paraffin Injection, Am. J. Surg. **19**:509, 1933.

processes extended far beyond the original site of the mass. The underlying fibrosis appeared to have been removed. The wound was closed with dermal sutures and healed by first intention.

Three weeks later a fibrotic mass seemed still to be present, but the deformity was reduced, leaving only a slight hypertrophic scar.

The left side showed a similar paraffinoma, 1½ inches (1.81 cm.) by ¾ inch (1.91 cm.), which did not extend to the nasal area. This mass was hard and also adherent to the subcutaneous tissue and orbital portion of the maxilla. On account of the difficulty encountered in attempting to dissect out the paraffinoma on the right side, I decided to use roentgen treatment. This was given in the dosage of 2 units of filtered roentgen rays through 2 mm. of aluminum (Mackee erythema dose) at biweekly intervals for three treatments.

When the patient was last seen on Oct. 9, 1934, the mass had disappeared, although some hard, possibly fibrotic areas could be palpated. The cosmetic result was much better than on the right side owing to the fact that there was no scar. Up to the present time there have been no sequelae as the result of the roentgen treatment.

COMMENT

Dermatologists as a group deprecate the use of paraffin for cosmetic purposes. It is difficult to evaluate the results from its employment, as statistics are not available and the dermatologist is consulted only when the results are unsatisfactory.

Is the judicious use of paraffin successful in the hands of competent physicians? S. Mort [2] has used solid paraffin (melting point between 110 and 115 C.) to replace lost tissue. He makes an opening and inserts the substance in the lesion. In certain cases he claims good results.

The treatment of patients in whom a deformity has developed from the use of paraffin is varied. Results are not encouraging. The following methods have been tried:

1. Surgical excision. This procedure should include complete excision of the overlying skin and tissue. The area so removed should be replaced by a gratt if necessary. An attempt to cut over the mass and dissect out the tissue does not give satisfactory results because fibrosis extends far beyond the overlying cutaneous area. Usually the dissection is not complete, and the fibrosis with the cicatrization leaves a marked deformity.

2. Radiotherapy and treatment with the high frequency current. These were used by Gaskell [3] with success. Both Sutton [4] and Ormsby [5] have reported success with the use of radium.

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2. Mort, S.: Use of Solid Wax, Lancet **2**:105 (July 19) 1919.

3. Gaskell, quoted by Ormsby,[5] p. 568.

4. Sutton, Richard L.: Diseases of the Skin, ed. 6, St. Louis, C. V. Mosby Company, 1926, p. 687.

5. Ormsby, Oliver S.: Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1921, p. 568.

3. Treatment with the galvanic current and the incandescent bulb. Schamberg [6] used the galvanic current and the incandescent bulb and was under the impression that the heat produced the desired effect by dissolving the paraffin. However, ordinary heat and the galvanic current will not dissolve or soften the fibrosis which is present.

4. Roentgen treatment. This was used by Williams [7] with success. Sutton [4] had no success with this therapy.

MacKee,[8] in a discussion of a case of paraffinoma, stated that paraffin acts as a foreign body and that the tissues will rebel in time and give an inflammatory reaction.

Oppenheimer [9] and Davis [10] both stated the belief that there is a distinct risk in using paraffin intradermally.

No preparations of petroleum, paraffin oil or wax taken internally or applied externally have been proved so far to be detrimental.[11]

Photograph showing paraffinomas of the right and left lower eyelids. The right lid shows a cicatrizing scar following the excision. The left lid shows a similar lesion treated by roentgen rays.

The question naturally arises whether persons react differently to foreign bodies with overproduction of tissue cells and giant cell formation. Will cells so stimulated become malignant, or are these cells potentially malignant with or without the carcinogenic factor of the foreign body? Paraffin is a product of coal tar, which is known to be carcinogenic. In a suitable area or environment, it is possible that a paraffinoma may produce a cell that ultimately will become malignant.

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6. Schamberg, J., quoted by Ormsby,[5] p. 568.

7. Williams, quoted by Ormsby,[5] p. 687.

8. MacKee, George M., in discussion on Kingsbury.[17]

9. Oppenheimer, S.: Condemnatory Note on Use of Paraffin in Cosmetic Rhinoplasty, Laryngoscope **30**:595 (Sept.) 1920.

10. Davis, B. F.: Paraffinoma and Wax Cancer, J. A. M. A. **75**:1709 (Dec. 18) 1920.

11. White, R. Prosser: The Dermatoses or Occupational Affections of the Skin, ed. 3, New York, Paul B. Hoeber, Inc., 1928, p. 252.

The lighter extracts from distillation of crude oils do not have a keratogenic or a carcinogenic influence.[12] This action seems to be confined to products of the second and third distillations. Bridge[13] stated that he had never observed carcinoma to develop in a candle maker. Ullman[14] stated that when paraffin is used as a bleach, injury to the skin is a negligible consideration, and dermatoses from paraffin have been reduced to a minimum. Abscesses have devoloped when the lesion has produced necrosis from pressure on the overlying epidermis (fig. 1).

Stokes and Scholl[15] and Schamberg[16] reported cases of cancer developing in workers handling paraffin. In a discussion of a case observed by Kingsbury,[17] Wise stated that he saw a sarcoma develop from a paraffinoma which had been diagnosed previously as sarcoid.

Weidman[18] called attention to the development of paraffinomas in patients in whom paraffin had been used as the vehicle for intramuscular injections of bismuth, camphor or mercury.

CONCLUSIONS

Although the report of a single case of paraffinoma with the successful use of roentgen treatment has its drawbacks in not being conclusive evidence, the procedure is not too dangerous to be employed with the dosage used in this case. The cosmetic result is much better than that obtained with either excision or dissection. Some tissue is recalcitrant to the effects of the roentgen rays; nevertheless, the treatment should be attempted at intervals of sufficient length so that observations on whether or not it will be effective may be made. In this manner, the resistant type of lesion will be noted and the harmful effects of overexposure to roentgen rays will be avoided.

5050 Jenkins Arcade.

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12. White,[11] p. 253.

13. Bridge, quoted by White,[11] p. 252.

14. Ullman, quoted by White,[11] p. 253.

15. Stokes, J. H., and Scholl, A. J., Jr.: Probable Paraffin-Oil Tumor, Arch. Dermat. & Syph. **4**:50 (July) 1921.

16. Schamberg, J.: Cancer in Tar Workers, J. Cutan. Dis. **28**:644, 1910.

17. Kingsbury, J.: Paraffinoma [Case Report], Arch. Dermat. & Syph. **1**:737 (June) 1920.

18. Weidman, F.: The Danger of Liquid Petrolatum in Parenteral Injections, J. A. M. A. **80**:1761 (June 16) 1923.

GENERALIZED PUSTULAR PSORIASIS

REPORT OF A CASE

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There have recently appeared in the literature a number of reports of cases of a condition considered to be a pustular form of psoriasis, in some of which the patients presented typical psoriatic in addition to pustular lesions, and in others of which the diagnosis was based chiefly on the microscopic changes. There has been a great deal of controversy as to whether these are really cases of psoriasis, a number of dermatologists contending that they are instances of acrodermatitis continua of Hallopeau and that typical psoriatic lesions, when present, are merely incidental. It appears that it will be necessary to observe a large number of cases of eruptions of this type to attain a general conformity of opinion. I wish to report a case belonging to this group.

REPORT OF CASE

E. G., a white man aged 53, was admitted to the Knickerbocker Hospital on Dec. 12, 1932, with a complaint of pain and swelling of the joints of the feet, ankles, hands and wrists. The feet and ankles had been involved for three weeks and the hands and wrists for three days. In each instance within a day of the onset an eruption had appeared on the involved area.

The family history was unimportant.

The past history revealed that the patient had had attacks similar to the present one in 1927 and 1929. On those occasions, according to the patient's description, the condition was identical to that described here. Both the arthritic and the dermatologic manifestations had been present, and in each instance the duration had been between four and five months. The patient reported that between the attacks there had been scaly patches on the elbows and the scalp. The venereal history was irrelevant. The appendix had been removed about fifteen years before. The teeth had been carious, and all except a few front teeth had been removed. The patient had been partially deaf for about fifteen years, but this condition had not progressed during the past five years. Examination on admission to the hospital gave the following results:

Cutaneous Involvement.—The hands, wrists and feet presented erythematous, scaly, pustular patches varying in size from 0.5 to 2 cm., many of which coalesced. In general, the dorsal aspects were the more completely involved. The pustules, which varied from the size of a pinhead to about twice that, were discrete and distributed among the scales; some of them had a superimposed crust. The greatest number of pustules was at the periphery of the patches, bordering on normal

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From the Department of Medicine, Knickerbocker Hospital, service of Dr. Fred P. Solley; Dr. Edward H. Rogers, medical director.

skin. Rupture of some of the pustules had caused a purulent oozing, which suggested, particularly between the toes, a mycotic condition with secondary infection. The scalp and the extensor surfaces of the elbows presented irregular patches of silvery scales. On removal of the scales the bleeding points typical of psoriasis could be demonstrated. The pubis, the scrotum, part of the shaft of the penis and the groins presented erythematous, scaly, moist plaques with irregular borders, most of which were confluent. There was considerable maceration in the folds of the skin. The eruption extended to the adjacent areas of the thighs for a distance of about 10 cm.

The nails of the fingers and toes presented stippling, longitudinal grooving and brownish discoloration. The free edges were raised and cracked in places, and there were heaped-up crusts beneath them.

General Physical Examination.—On the patient's admission the temperature was 100.4 F., the pulse rate was 88, and the respiratory rate was 24. The temperature ran an irregular course until Jan. 1, 1933, during which time it ranged between 99 and 102.2 F. There was a tendency toward an elevation of the temperature in the evening. During this time the pulse rate ranged from 72 to 108 and the respiratory rate from 20 to 24. On January 5 the temperature, pulse rate and respiratory rate reached approximately normal levels and remained there until the patient was discharged on January 19. The joints of the hands and wrists were moderately swollen and red. Pressure over these joints elicited marked tenderness, and there was definite limitation of motion. There was some swelling of the joints of the ankles and feet, with moderate tenderness. The patient was definitely hard of hearing. All of the teeth were missing. The pharynx was not injected. There was no evidence of diseased tonsils. The heart sounds were weak but regular, and there were no thrills or murmurs. The signs in the lungs were normal. The scar of a McBurney incision was visible. There were no other abdominal findings. Neurologic findings were not significant. The severity of the acute involvement of the joints followed closely the course of the temperature, as well as the cutaneous eruption.

Roentgen examination of the hands on January 17 revealed considerable atrophy of several bones of each hand and subluxation of nearly all the interphalangeal articulations. The condition was most marked in the proximal interphalangeal articulation of the fifth digit of each hand and in the proximal articulations of the second and fourth digits of the left hand. On the opposing surfaces of the articulations were atrophic changes to the most marked degree. There was an erosion of the distal articular surface of the middle phalanx of the right hand near the ulnar aspect.

Electrocardiographic examination revealed normal rhythm, with preponderance on the right and a rate of 105.

Chemical analysis of the blood showed 76.9 mg. of sugar per hundred cubic centimeters, 25 mg. of nitrogen, 0.8 mg. of creatinine and 5 mg. of uric acid.

The Wassermann reaction of the blood was negative.

Repeated examination of the urine gave negative results except for frequent faint traces of albumin and a few white blood cells.

Microscopic examination of the scales from the hands and feet failed to reveal fungi. Scrapings from the shaft of the penis revealed no fungi or Ducrey's bacilli. Microscopic examination of scrapings from the nails, prepared with a 20 per cent solution of potassium hydroxide, revealed no evidence of mycotic involvement. Cultures of the nails were also negative. Four cultures from the pustules were taken under sterile precautions. Two of these showed the presence of Staphylococcus aureus, but the other two were sterile.

Intradermal tests with trichophytin in dilutions of 1 : 20 and 1 : 10 were negative.

The blood count showed: 3,850,000 erythrocytes; 75 per cent hemoglobin and 7,950 leukocytes, with 67 per cent polymorphonuclear neutrophils, 12 per cent basophils, 1 large mononuclear and 30 per cent lymphocytes. On December 22, when the temperature reached 102.2, the leukocyte count rose to 11,300, with 78 per cent polymorphonuclear neutrophils. On January 9, when the temperature had been normal for several days, the count was 6,600, with only 48 per cent polymorphonuclear neutrophils.

Progress of the Eruption.—On the hands, the wrists and feet repeated crops of pustules similar to those present on admission appeared during the first five

Fig. 1.—Appearance of the eruption about one month after the patient's admission to the hospital. Note the approximate symmetry of distribution, the involvement of the nails and the predominance of scales, with a few pustules. The nail of the third finger of the right hand had fallen off.

weeks of observation, gradually decreasing in number and leaving only crusts and silvery scales. Figures 1, 2 and 3 were taken about one month after admission and show a predominance of crusts and silvery scales, although a number of pustules are discernible. There was pus under some of the crusts. Treatment consisted at various times in applications of boric acid solution, potassium permanganate (1: 3,000) and an ointment containing 5 per cent sulphonated bitumen and 5 per cent ammoniated mercury. None of these appeared to influence the course of the eruption. The patient was discharged from the hospital on January

19, at which time no pustules remained though there were numerous patches of scales and a few crusts.

I have observed this patient since he left the hospital. The lesions just described gradually faded and completely disappeared about May 1, approximately five months after the onset. Up to the present time there has been no recurrence.

The typical psoriatic lesions on the elbows and scalp were treated with an ointment containing 10 per cent ammoniated mercury. They cleared completely after two months, but recurred about one month later. Within about two weeks a few pustules appeared in the lesions on the elbows and disappeared several weeks later. With further treatment the scaling on the scalp and elbows cleared

Fig. 2.—Photograph taken at the same time as figure 1. Note the heaped-up crusts beneath some of the nails. Pustules, crusts and scabs are discernible.

but again recurred. Owing, probably, to the patient's failure to continue regular applications of the mercury ointment, these lesions have been present up to the time of writing.

The involvement of the pubic area, groins, scrotum and shaft of the penis made very little response to a number of applications. The lesions finally became less pronounced and disappeared at the same time as the eruption on the hands and feet.

One finger-nail and one toe-nail fell off about two months after the onset of the condition, but both were shortly replaced by new nails, which took on the characteristics of psoriatic nails.

Fig. 3.—A few pustules and many scales. The similarity of the appearance of this condition and a mycotic infection may be observed.

Fig. 4.—Typical psoriatic lesions on one elbow, taken at the same time as the previous figures. The appearance of the other elbow was practically identical. Later a few pustules developed in these lesions.

Histopathologic Study.[1]—A section taken on Dec. 31, 1932, from the dorsal surface of the left foot, including pustules the size of a pinhead, revealed the following features: There was thickening of the stratum corneum with the presence of a number of clear linear spaces and slight parakeratosis. In one area corresponding to the pustule discernible clinically (fig. 5) was a large collection of leukocytes walled off sharply by the prickle cell layer with a complete absence of the stratum granulosum. These leukocytes were chiefly polymorphonuclears with a few lymphocytes. In the remainder of the section the stratum granulosum was partially absent (fig. 6). Immediately adjacent to the pustule the epidermis

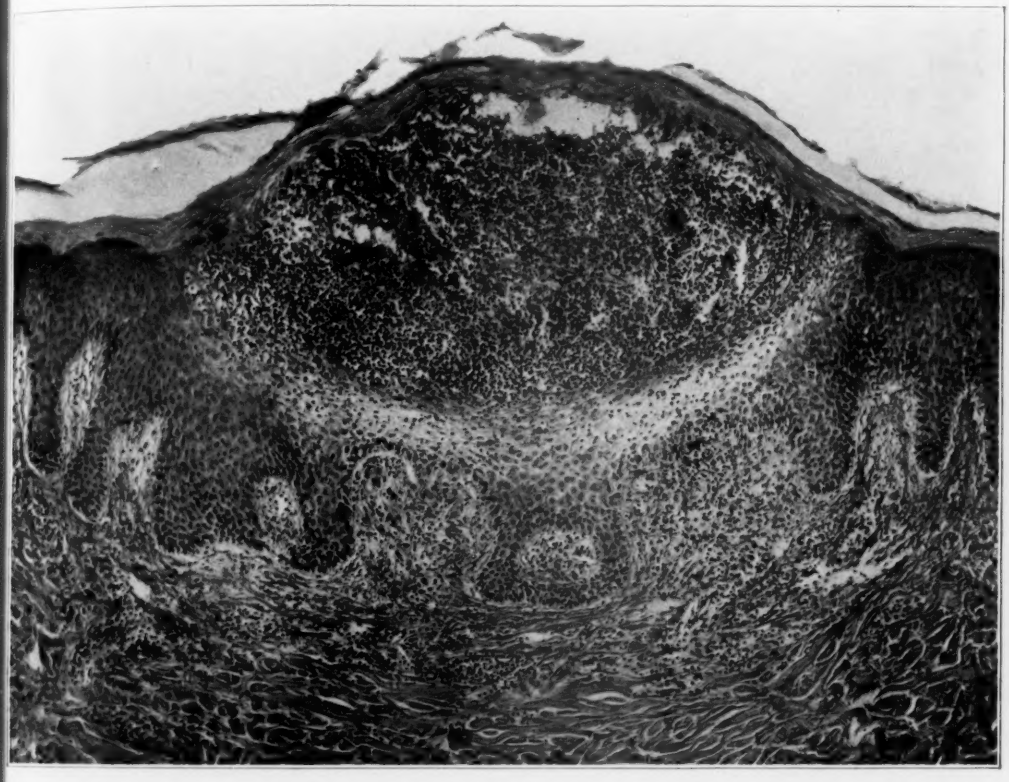

Fig. 5.—A section from the dorsum of the left foot, showing a pustule, linear clear spaces in the stratum corneum, slight parakeratosis and acanthosis.

was practically normal, although there was for the most part distinct acanthosis. Some of the superpapillary portions of the epidermis presented a thinning out of the prickle cell layer.

In the corium beneath the pustules the papillae showed definite widening of their distal ends with corresponding edema. There was moderate cellular infiltration by round cells, polymorphonuclears and a few epithelioid cells. In the subpapillary layer there was moderate perivascular infiltration by similar cells.

1. Dr. John Frank Fraser advised me in the preparation of this histopathologic study.

A biopsy specimen of a lesion from the left elbow, at which time there were no pustules, presented the typical histologic picture of psoriasis.

According to McCarthy,[2] although the stratum granulosum is usually absent in psoriasis vulgaris, it is not uncommon to find patches of pure hyperkeratosis with an underlying wider or normal keratohyaline layer. He stated that "the collection of leukocytes in the epithelium is always in proportion to the intensity of the process, and, in some cases, it may be so extensive as to warrant the name psoriasis pustulosum."

MacKee[3] stated that the biopsy specimens of pustular psoriasis taken during a pustular and inflammatory exacerbation present nothing that conforms to the

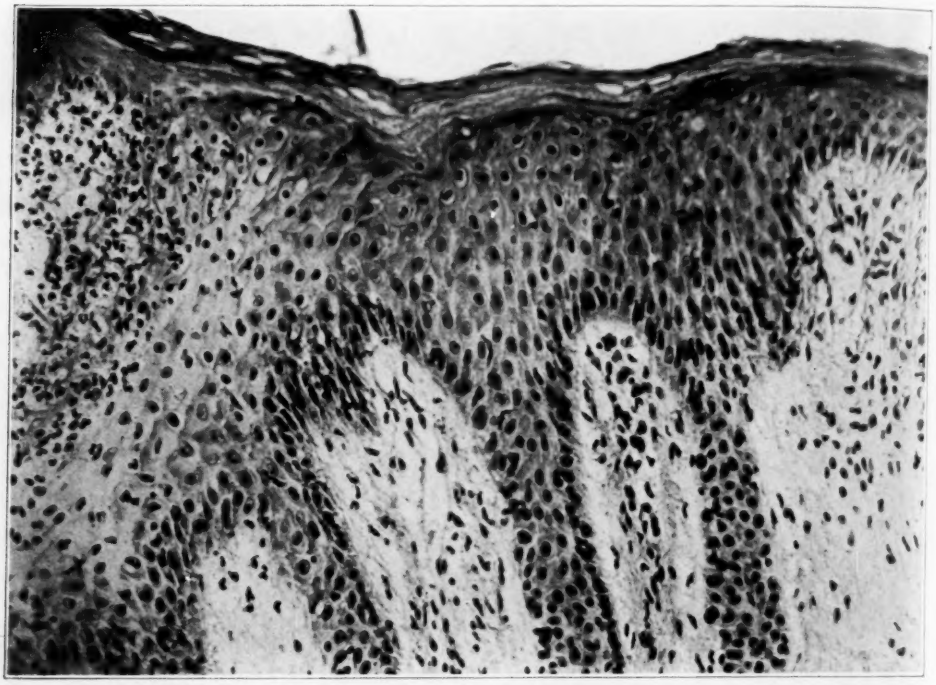

Fig. 6.—A portion of the section shown in figure 5, including an enlargement of a corner of the pustule (left). Note the collection of leukocytes (chiefly polymorphonuclears), lengthening of the papillae with widening of their distal ends, leukocytic infiltration and vascular dilatation and the thinning of the portion of the prickle cell layer above the papilla at the extreme right.

typical histologic picture of psoriasis. He expressed the belief that the sections from lesions which present the histopathologic picture of psoriasis must be taken between exacerbations, during the squamous stage, when there are few or no pustules.

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2. McCarthy, Lee: Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, p. 196.

3. MacKee, George M.: Psoriasis Pustulosa, Arch. Dermat. & Syph. **30**:161 (July) 1934.

COMMENT

The literature on pustular psoriasis has been completely and admirably reviewed by Barber [4] and Ebert,[5] both of whom have described in detail the differential features between this dermatosis and acrodermatitis continua of Hallopeau. Although it was previously considered that staphylococci are always present in cases of acrodermatitis continua, it has been shown that the pustular lesions in that dermatosis may be absolutely sterile.[6] On the other hand, in accepted cases of pustular psoriasis, as in that reported by MacKee,[7] the presence of staphylococci has been demonstrated in cultures from the pustules.

The condition in the case which I have reported resembled in many ways that in Barber's case 2. Points in common were systemic reaction with considerable elevation of temperature and polyarthritis during the pustular stage; a widespread distribution of the lesions and the presence of typical psoriatic lesions during and between pustular manifestations. However, in this case of Barber's there developed generalized exfoliative dermatitis of the pityriasis rubra type. In his other cases there were some features in common with those in my case, namely, the presence of both ordinary and pustular psoriatic lesions, periodic acute exacerbations, exact bilateral symmetry, the absence of suppurative paronychia and involvement of the nails typical of psoriasis.

According to Barber, there is a type of pustular psoriasis of generalized distribution with the formation of pustules in other areas as well as on the palms and soles. In a great many of the cases of pustular psoriasis which have been reported the pustular lesions have been limited to the palms and soles, some with no typical psoriatic lesions elsewhere.

I believe the condition in Ebert's case 1 corresponded quite closely to that in my case. The following features in common are obvious: 1. There were definite phases of cutaneous activity with associated systemic reaction. On first observation the condition in my case seemed to correspond to Ebert's late "subacute phase" and then proceeded to the "acute phase." An "interim phase" has apparently been present for the past year, during which time only a few resistant psoriasiform plaques have been present on the elbows and on the scalp. According to the history, similar phases existed before the last attack and between

4. Barber, H. W.: Acrodermatitis Continua Vel Perstans (Dermatitis Repens) and Psoriasis Pustulosa, Brit. J. Dermat. **42**:500 (Nov.) 1930.

5. Ebert, Michael H.: A Psoriasiform Eruption with Pustular Exacerbations, Arch. Dermat. & Syph. **27**:933 (June) 1933.

6. Ruiter, M.: Dermatite exfoliative généralisée à terminaison mortelle au cours de l'acrodermatite continue d'Hallopeau, Ann. de dermat. et syph. **7**:231, 1933.

7. MacKee, George M.: Psoriasis Pustulosa, Arch. Dermat. & Syph. **27**:1045 (June) 1933.

the previous ones. 2. There were moist plaques of the intertrigenous type involving the crural region, the scrotum and the shaft of the penis during the acute and subacute phases. These corresponded to the intertriginous eruption under the breasts and around the vulva in Ebert's case. 3. All the nails were involved. 4. Associated acute polyarthritis was present. The condition in Wrong's [8] case of pustular psoriasis resembled that in the case which I have described, except that in his the pustular eruption on the hands and feet was less extensive and there was no intertriginous involvement. The microscopic observations were similar.

De Wolf [9] reported a case of pustular psoriasis with destructive arthritis of the joints of the fingers.

Milian and Katchoura [10] reported a case of psoriasis with an acute generalized pustular stage during which there was a pronounced systemic reaction. They concluded that in cases of this type the existence of pustules does not constitute a complication of psoriasis but represents a distinct variety of that dermatosis.

In fifteen cases reported by Andrews, Birkman and Kelly [11] there were pustular lesions of the palms and soles with some features similar to those in the cases just described, but there were no typical psoriatic lesions, no changes in the nails and inconclusive histopathologic observations. The authors considered that they lacked sufficient evidence to include these cases as instances of pustular psoriasis. Numerous cases similar to these have recently been reported as instances of pustular psoriasis, and as yet there is little conformity of opinion.

The confusion which exists regarding the classification of pustular psoriasis as an entity may be gathered from a discussion at a meeting of the Royal Society of Medicine (Section on Dermatology).[12] Barber, Roxburgh and Dowling agreed that the pustular form of psoriasis is a definite entity. Barber described a case in which he had given treatment a number of times for severe ordinary psoriasis and in which pustular lesions developed on the hands and, later, in patches of ordinary psoriasis on the elbows. Three distinguished members of the society maintained

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8. Wrong, Norman M.: Pustular Psoriasis, Arch. Dermat. & Syph. **28**:682 (Nov.) 1933.

9. De Wolf, H. F.: Pustular Psoriasis with Arthritis of the Fingers, Arch. Dermat. & Syph. **26**:587 (Sept.) 1932.

10. Milian, G., and Katchoura, V.: Psoriasis pustuleux généralisé, Bull. Soc. franç. de dermat. et syph. **40**:85, 1933.

11. Andrews, George C.; Birkman, Frederick W., and Kelly, Richard J.: Recalcitrant Pustular Eruptions of the Palms and Soles, Arch. Dermat. & Syph. **29**:548 (April) 1934.

12. Barber, H. W.: Presentation of a Case of Pustular Psoriasis of the Extremities, Brit. J. Dermat. **45**:113 (March) 1933.

that there is no such entity as pustular psoriasis and that in cases so named there are usually two dermatoses—ordinary psoriasis and a pustular eruption, frequently acrodermatitis continua of Hallopeau.

SUMMARY AND CONCLUSIONS

A case of generalized pustular psoriasis with typical psoriatic patches during and between pustular attacks is described. The patient presented also acute arthritis during pustular attacks, with resulting articular destruction. In a history of three attacks an increase in the number of typical psoriatic lesions, the appearance of numerous pustular lesions and acute arthritis have been concomitant. All the nails were involved and presented the typical features of psoriasis.

Acrodermatitis continua was ruled out by the distribution of the lesions, the clinical course and the microscopic observations. The question of the pustules' being sterile or containing staphylococci is no longer considered of importance in differentiating between these two conditions.

Mycotic infection was ruled out by bacteriologic examination of the skin and nails as well as by the trichophyton test.

I believe that the observations in this case are sufficient to warrant a diagnosis of pustular psoriasis of the generalized type.

565 Park Avenue.

ARSENIC AS AN ETIOLOGIC AGENT IN CERTAIN TYPES OF EPITHELIOMA

DIFFERENTIAL DIAGNOSIS FROM, AND FURTHER STUDIES REGARDING, SUPERFICIAL EPITHELIOMATOSIS AND BOWEN'S DISEASE

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The purpose of this paper is to distinguish between superficial epitheliomas precipitated by, or resulting from, ingestion of, or exposure to, arsenic and superficial epitheliomatosis and Bowen's disease. The incidence and relative malignancy of these epitheliomas will be considered either in association with arsenical keratosis or independent of it. The literature has been reviewed, including about a thousand articles read in the last ten years on the subject of epithelioma and precancerous dermatosis, but reference is made only to recent or more pertinent articles.

MATERIAL FOR STUDY AND PROCEDURE

This study is based on a review of all the cases of arsenical keratosis and superficial epithelioma of the trunk and extremities seen in the section on dermatology of the Mayo Clinic from 1918 to 1934 and includes eighty-five cases of arsenical keratosis, in sixteen cases of which the arsenical type of epithelioma was present; two cases of arsenical type of epithelioma simulating Bowen's disease; five cases of Bowen's disease, and forty-one cases of superficial epitheliomatosis. The classification of the cases was dependent not only on an analysis of the history of the clinical findings, in the majority of cases confirmed by histopathologic studies, but in nineteen of the more recent cases it depended also on the results of chemical studies for arsenic in urine, hair and tissue.

The determinations of arsenic were made by Osterberg's [1] method on urine, hair and pieces of tumor tissue from which the subcutaneous fat had been removed. I also used Osborne's [2] method of demonstrating crystals of arsenic trisulphide in

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From the Section on Dermatology and Syphilology, The Mayo Clinic.

Read at the Fifty-Seventh Annual Meeting of the American Dermatological Association, Inc., New York, June 7, 1934.

1. Osterberg, A. E.: A Modification of the Electrolytic Gutzeit Apparatus for the Estimation of Arsenic in Biological Material, J. Biol. Chem. **76**:19 (Jan.) 1928.

2. Osborne, E. D.: Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, Arch. Dermat. & Syph. **12**:773 (Dec.) 1925; Microchemical Studies of Arsenic in Arsenical Dermatitis, ibid. **18**:37 (July) 1928. Osborne, E. D.; Putnam, E. D., and Hitchcock, Blanche S.: The Effect of Arsenic on

histologic sections. The latter method is sensitive and permits of accurate visualization of the location of the arsenical deposit; my good opinion of the method is not in accord with that of Tannenholz and Muir.[3] It is important to distinguish the fine crystals of arsenic trisulphide, with their greenish halo, from particles of fat of various sizes and from extraneous substances found in the stratum corneum, including particles of steel deposited from the microtome knife. Granules of melanin pigment in the epidermis or cutis lack the refractility of arsenic trisulphide crystals.

Depending on the locality in which the patient lives, his occupation and the type of food ingested, arsenic may be present normally in the urine to the extent of 1 mg. in each liter and, according to Billeter and Marfurt,[4] in the hair and skin in amounts up to 0.0097 mg. per hundred cubic centimeters. Conversely, a single negative result of a test of the urine for arsenic may be without significance, as was exemplified by cases in which the presence of arsenic was subsequently demonstrated. I have also demonstrated the presence of arsenic in pathologic amounts by Osborne's and by Osterberg's method in the tissue obtained in cases of various types of dermatosis, without there being clinical evidence of the effect of arsenic in the form of pigmentation, keratosis or malignant change. Neither Osborne [5] nor I have been able to demonstrate arsenic in the skin of certain patients who had been taking arsenic for some time, and in persons with typical arsenical keratosis the results of chemical tests for arsenic by both methods may be negative.

That arsenic in the inorganic or pentavalent form has an affinity for the epidermis has been amply demonstrated by the work of Osborne [2] and by the experimental production of epithelioma by Leitch and Kennaway.[6] Contrary to the prevailing impression, trivalent forms of arsenic may have an affinity for the epidermis. Ebert [7] has shown that the application of arsphenamine to the skin may produce histologic changes simulating those of Bowen's disease. Rare cases of arsenical keratosis which resulted from injections of arsphenamine (trivalent arsenic) have been reported.

Rabbits: Microchemical Studies Following the Administration of the Arsphenamines and Tryparsamide, ibid. **25**:419 (March) 1932. Montgomery, Hamilton, and O'Leary, P. A.: Pigmentation of the Skin in Addison's Disease, Acanthosis Nigricans and Hemochromatosis, ibid. **21**:970 (June) 1930.

3. Tannenholz, Harold, and Muir, Kathleen B.: Methods for Microchemical Demonstration of Arsenic in Tissues, Arch. Path. **15**:789 (June) 1933.

4. Billeter and Marfurt, quoted by Mayer.[9]

5. Osborne, E. D.: Personal communication to the author.

6. Leitch, Archibald, and Kennaway, E. L.: Experimental Production of Cancer by Arsenic, Brit. M. J. **2**:1107 (Dec. 9) 1922.

7. Ebert, M. H.: Die histologischen Veränderungen nach einmaliger Salvarsanapplikation in der Haut, Arch. f. Dermat. u. Syph. **158**:365, 1929.

ARSENICAL KERATOSIS

The literature regarding arsenical keratosis was recently reviewed by Ullmann,[8] Mayer[9] and Kennaway[10] and the histologic-pathologic changes have been described by Waelsch.[11] The clinical appearance of the lesions on the palms, fingers, soles, and toes is distinctive and can be confused only with hereditary conditions, such as keratoma punctata. Occasionally only the palms or the soles are involved. In one of my patients arsenical keratosis appeared on the backs of the hands but not on the palms and soles. Arsenical keratosis of the palms and soles was found in this series of eighty-five cases to be a result of exposure to, or ingestion of, arsenic in the following conditions: It occurred in psoriasis in nineteen cases, but with no relation of the psoriatic lesions to epithelioma, and in dermatitis herpetiformis and eczema in eight cases each. It was associated with superficial epitheliomatosis in seven cases (including one case in which psoriasis was also present and which is listed with the nineteen cases of psoriasis); occupation and psychoneurosis in five cases each; syphilis in four cases, in none, however, traceable to treatment with arsphenamine, but representing older forms of treatment with pentavalent or inorganic forms of arsenic; pernicious anemia, migraine and epilepsy in two cases each; the taking of a tonic that contained arsenic in two cases; acne, asthma, leukemia, dermatitis repens, Parkinson's disease, St. Vitus' dance and lichen planus in one case each. In one case arsenic was taken for the improvement of the complexion. In one additional case chronic arsenicalism developed as a result of the use of a contaminated water supply. There were thirteen cases in which there was no definite history of treatment with arsenic.

The average age of onset of arsenical keratosis was 44 years; the youngest patient, aged 11 years, had had keratosis for nine months, and the oldest patient, aged 74 years, had had the lesions for two years. There was an average of three males to one female. Arsenical pigmentation was associated with the keratosis in about one-half the cases.

8. Ullmann, Karl: Neueres über das As-Carcinom; VIII. Comptes rendus Congrès international de dermatologie et de syphiligraphie, Copenhagen, Engelsen and Schroder, 1931, p. 693; Krebsbildung in der Gewerbemedizin und ihre Beziehungen zur experimentellen Geschwulstforschung, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, pts. 2 and 3, p. 551; Beruflich industriell enstandene Blastombildung und allgemeine Krebsforschung, Dermat. Wchnschr. **97**:1019 (July 8) 1933.

9. Mayer, R. L.: Toxicodermien, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 4, p. 40.

10. Kennaway, E. L.: The Anatomical Distribution of the Occupational Cancers, J. Indust. Hyg. **7**:69 (Feb.) 1925.

11. Waelsch, Ludwig: Zur Histologie der Arsenkeratose, Arch. f. Dermat. u. Syph. **86**:245, 1907.

The arsenical keratosis might develop within a month after the first ingestion of arsenic or not until thirty years after medication had been stopped. Once developed, the keratosis in some cases persisted and progressed until an epitheliomatous change developed in spite of the cessation of administration of arsenic, but in many cases gradual involution of the keratosis occurred after the use of the drug had been stopped. The arsenic was administered in the form of solution of potassium arsenite, U. S. P. (Fowler's solution), in the majority of cases. Neither the amount of arsenic taken nor the length of time over which it was taken seemed to have any bearing on the result. Thus, one patient took solution of potassium arsenite steadily for more than twelve years with only mild pigmentation and keratosis resulting, whereas in another case arsenical epithelioma of the palms and soles eventually developed as the sequel of the ingestion of small amounts of solution of potassium arsenite taken by mouth for one month twenty years previously. Epithelioma developed in 20 per cent of the cases, either in the keratotic lesions or as superficial epitheliomas elsewhere on the body. In nine cases superficial epitheliomas of the arsenical type were present on the trunk. Four patients apparently died as a result of arsenical epithelioma and metastasis, and one died of cirrhosis of the liver as the result of exposure to arsenic in his occupation.

In the early stages the histopathologic picture of arsenical keratosis may resemble that of verruca vulgaris, but early one sees phenomena of keratinization of individual cells leading to epitheliomatous changes and rather marked secondary inflammatory changes in the cutis. Eventually, all gradations from squamous cell epithelioma, grade 1, in situ, presenting microscopic features of Bowen's disease, to invasive squamous cell epithelioma, grade 3, can be seen. In the intra-epidermal stage of the epitheliomatous process, the picture differs from Bowen's disease only in that there are vacuolation of individual cells and a less marked tendency toward the formation of epithelial giant cells by amitotic cell division. I was unable to support the findings recorded in the literature that arsenical keratosis or epitheliomatous changes therein take place about the sweat ducts. I did not see evidence in any of the sections studied microscopically of basal cell epithelioma arising from arsenical keratosis, although this probably can occur, as it does in a few cases of senile keratosis. Radiotherapy is contraindicated in these cases, as is evidenced by case 1, to be reported in the following paragraphs, and by the fact that the histologic changes are similar to those seen in early epithelioma caused by roentgen rays or radium. Case 2 illustrates the relatively benign course in spite of malignant pathologic changes. Case 3 emphasizes the systemic injury that may result following the ingestion of arsenic and the subsidence of symptoms after the source of arsenic has been eliminated.

CASE 1.—A draftsman, aged 34, was admitted to the clinic in April 1933 because of mild psoriasis which started in 1924. Solution of potassium arsenite, 1 to 26 drops three times a day, had been prescribed, and the patient had taken from 40 to 48 ounces (from 1,200 to 1,450 cc.) of this solution in five years. Keratotic lesions on the palms and soles first appeared three years after he started to take the solution containing arsenic. In 1930 an infection on the sole of the right foot, diagnosed as papilloma, was treated with radium for two hours. It recurred in four months and was then diagnosed as arsenical keratosis. Further treatment with radium seeds and roentgen rays proved ineffective, and metastasis to the inguinal nodes was evident in November 1932, which was confirmed histologically at operation. In January 1933 amputation at the middle of the leg was performed. Within two weeks, lesions appeared in the right groin which increased in size in spite of high voltage roentgen therapy. Operation again was performed in April 1933.

The patient, when examined at the clinic, presented mild psoriasis; the lesions responded promptly to treatment. There were definite arsenical pigmentation on the trunk and a small number of typical arsenical keratotic lesions on the palms and on the sole of the remaining foot; one of the latter was an ulcerated keratotic lesion, histologically a squamous cell epithelioma, grade 2, in situ. Tissue from the right foot and from the inguinal node, removed elsewhere, was similar histologically. The patient had an ulcer near the anus and another of the scrotum, histologically squamous cell epithelioma, grade 2. Studies of a keratotic lesion excised from the left palm (histologically squamous cell epithelioma, grade 1) by Osborne's method revealed crystals of arsenic trisulphide, but direct chemical analysis yielded negative results for arsenic. The keratotic lesion was fulgurated, and further intensive roentgen therapy was applied to the inguinal lymph nodes, following which there were definite regression of the nodes and healing of the sinuses leading from them. The rectal lesion was treated with radium and healed without the formation of a scar.

The patient subsequently went elsewhere and because of recurrence of a mass in the right groin received further high voltage roentgen therapy and had a recurrence of the lesions about the anus, the buttocks and the scrotum. He died in January 1934 of secondary hemorrhage from the femoral vessels.

CASE 2.—A farmer, aged 42, was first seen at the clinic in February 1927 because of an epithelioma of the sole of the left foot (fig. 1*a*) which developed apparently from lesions of arsenic keratosis. He had been given medicine for the treatment of eczema, in the form of drops, for six years during early childhood. Amputation of the foot was advised but was not permitted; so simple excision together with application of radium to the enlarged inguinal nodes was employed.

Examination of the tissue revealed a squamous cell epithelioma, grade 3. Seven years later there was no recurrence of the epithelioma on the sole, but the patient had numerous superficial epitheliomas of the arsenical type on the trunk; these were of squamous cell type and were graded 1 and 2 on histologic examination. There was also one typical lesion of superficial epitheliomatosis, diagnosed clinically and confirmed histologically as a basal cell epithelioma. Direct chemical analysis of normal skin as well as of an area of arsenical epithelioma gave no evidence of arsenic, although Osborne's method disclosed crystals of arsenic trisulphide in several specimens of epithelioma of the arsenical type. The arsenic crystals were most marked in the areas where tumor existed. Studies of the hair for arsenic gave negative results.

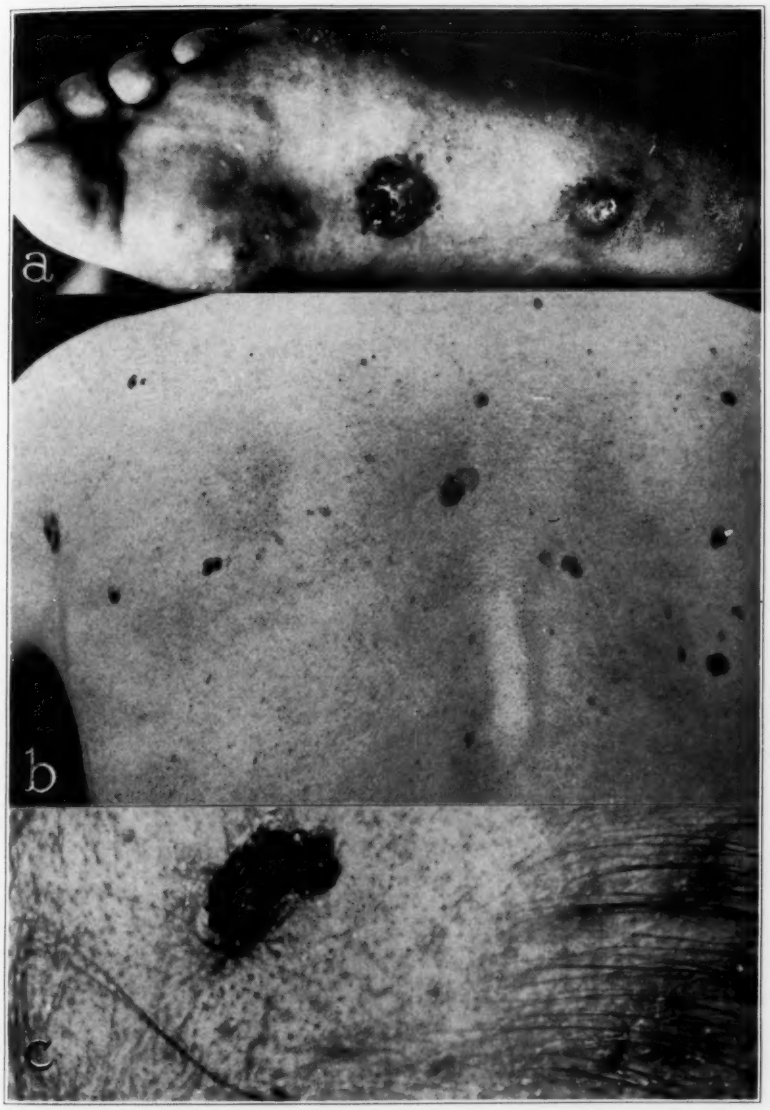

Fig. 1.—In *a* (case 2) is shown squamous cell epithelioma, grade 3, arising from lesions of arsenical keratosis, and in *b* (case 4), multiple superficial epithelioma of the arsenical type and smaller independent lesions of verruca senilis; in *c* (case 4) are depicted lesions on the scalp, with the characteristic, hard, verrucous crust covering a thick, rolled border. Smaller lesions, characteristic of the arsenical type of epithelioma, are present at the right.

The patient was seen again in February 1934, at which time he was found to have an intra-urethral epithelioma, grade 3; this was excised, and the penis was partially amputated.

CASE 3.—A married woman, aged 35, was first seen at the clinic in August 1931 because of progressive weakness and disability necessitating hospitalization. For the past two years she had noted increased pigmentation of the skin, associated with spells of acute vomiting and asthenia. Elsewhere, a diagnosis of possible Addison's disease had been made.

On examination there was evidence of cirrhosis of the liver, asthenia and low blood pressure (100 mm. of mercury systolic and 60 mm. diastolic). The patient presented a typical picture of arsenical pigmentation together with arsenical keratosis of the palms and soles and residual peripheral neuritis. A history of medication with arsenic could not be obtained. Urinalysis repeatedly disclosed large amounts of arsenic; as much as 1.4 mg. was found in 400 cc. of urine. There was 2.6 mg. of arsenic in 460 mg. of hair (5.6 mg. for each gram). Samples of water from the kitchen and bathroom faucets in the patient's home were sent to the clinic, and analysis revealed from 0.04 to 0.05 mg. of arsenic in a liter of water. The water gave a negative reaction for lead. Analysis of the tap water in the home of a physician living next door disclosed only 0.004 mg. of arsenic in a liter of water, and analysis of the city water supply revealed only 0.001 mg. in each liter. It was impossible to trace the source of arsenic further. It now became apparent that one daughter had died with symptoms of acute arsenicalism. The three remaining children were examined: The eldest son had 0.16 mg. of arsenic in 125 cc. of urine; the second son had 0.09 mg. in 150 cc. of urine, and examination of the daughter yielded negative results.

There was from 0.007 to 0.013 mg. of arsenic in each 400 mg. of the hair of the mother and of the three children. None of the children presented evidence of arsenical pigmentation or keratosis. The patient's husband gave no evidence either clinically or on examination of specimens of hair and urine of having ingested arsenic, presumably because his occupation as a traveling salesman kept him from being exposed to the arsenic in the water in sufficient quantities. The patient improved with rest in bed and a course of sodium thiosulphate. The family moved elsewhere, and two and a half years later the patient wrote that the pigmentation of the skin had entirely disappeared and that she was enjoying good health but that the arsenical keratosis still remained. None of the keratotic lesions had undergone malignant change.

ARSENICAL TYPE OF EPITHELIOMA

Whereas the picture of epitheliomatous change in arsenical keratosis is familiar, superficial epitheliomas occurring on the trunk precipitated by the ingestion of arsenic have not been generally recognized as arsenical epitheliomas but have been confused with lesions of superficial epitheliomatosis. These lesions are characterized clinically by their multiplicity and vary from ill defined, seborrhea-like crusts (fig. 1*b* and *c*) to lesions several centimeters in diameter covered with thick, tenacious, verrucous, hard, dirty crust, the removal of which reveals a wide, rolled, pearly border and appreciable induration, in contrast to a lesion of superficial epitheliomatosis, which has a fine, threadlike, elevated border. Lesions of arsenical epithelioma tend to simulate lesions of arsenical keratosis. In few of the cases was there clinical

or histologic evidence of arsenical pigmentation. In sixteen cases of arsenical epithelioma there were associated keratotic lesions on the palms and soles, and in seven of these there were associated lesions of superficial epitheliomatosis. Two cases of arsenical epithelioma simulating the clinical picture of Bowen's disease are more difficult to classify, as there was no evidence of arsenical keratosis or pigmentation, although arsenic was demonstrated in the epitheliomas and both the patients gave a history of the ingestion of arsenic. The histopathologic picture of superficial arsenical epithelioma on the trunk and extremities corresponds to that seen in epithelioma arising from arsenical keratosis. Basal cell epithelioma was seen in only one of a great many of these lesions that were studied histopathologically. Histochemical studies of several epitheliomas of squamous cell type disclosed arsenic in pathologic amounts, with more in the epithelioma than in the adjacent normal skin.

CASE 4.[12]—A farmer, aged 63, came to the clinic in November 1933. He feared cancer because several members of his family had died of carcinoma of various organs, although none of them had had epithelioma of the skin. A "wart" on the left ring finger had become an epithelioma, necessitating its amputation six years before the patient came to the clinic. Lesions had been present on the trunk for six or seven years. They started as reddish, crusted, scaling papules and gradually enlarged to a diameter of from 1.5 to 2 cm., forming a heavy, hard crust. A lesion on the scalp had recently been treated with roentgen rays.

Examination revealed, on both palms and on the fingers, typical lesions of arsenical keratosis, some of which had undergone epitheliomatous change. There were no keratotic lesions on the feet or any evidence of arsenical pigmentation. On the trunk were more than fifty epitheliomas of various sizes and stages of development (fig. 1*b*). There were also a crusted lesion on the scalp, about 1 cm. in diameter, and two smaller, superficial, scaling areas adjacent thereto (fig. 1*c*). Removal of the crusts of the larger lesions disclosed wide, rolled, pearly borders. There were no palpable lymph nodes. Specimens for biopsy were taken from eleven of the epitheliomas; all were squamous cell epitheliomas, grades 1 to 4 (fig. 2*a* to *d*). The arsenical keratotic lesions of the palms were histologically squamous cell epitheliomas, grades 1 and 2, in situ, with changes similar to those seen in Bowen's disease. A basal cell epithelioma was present in only one specimen, in a small area where it was apparently changing into a squamous cell epithelioma, grade 1, in situ. Numerous discrete lesions of verruca senilis were also seen on the back, but none showed clinical or histologic evidence of epitheliomatous change. Osborne's method of testing for arsenic, applied to the keratotic lesions of the hands and to several of the epitheliomas of the trunk revealed deposits of arsenic crystals, most marked in the epitheliomatous portions but appearing also in normal

12. Cases similar to this have been described in the literature by Guggenheim (Guggenheim, Lothar: Arch. f. Dermat. u. Syph. **168**:26, 1933), Mayer[9] (his figure 8, page 55) and O'Donovan (O'Donovan, W. J.: Brit. J. Dermat. **36**:477 [Nov.] 1922). Wende's case (Wende, G. W.: J. Cutan. Dis. **26**:531 [Dec.] 1908), reported as one of keratosis follicularis resulting in multiple epithelioma, I believe, is an example of the arsenical type of epithelioma, the histologic pictures being characteristic of squamous cell epithelioma, grades 1 and 3.

Fig. 2 (case 4).—Photomicrographs showing: *a*, arsenical keratosis of the finger, squamous cell epithelioma, grade 1, in situ, with individual cell keratinization; *b*, squamous cell epithelioma, grade 3, from the thorax, revealing the verrucous and invasive character of the lesion, including mitotic and amitotic cell division, dyskeratosis and vacuolation of the cells; *c* lesion from the left shoulder, showing vacuolation of cells and changes of the type seen in Bowen's disease, in an early squamous cell epithelioma, grade 1, in situ, and *d*, squamous cell epithelioma, grade 4, from the scalp. Narrow strands of undifferentiated cells and giant tumor cells are present.

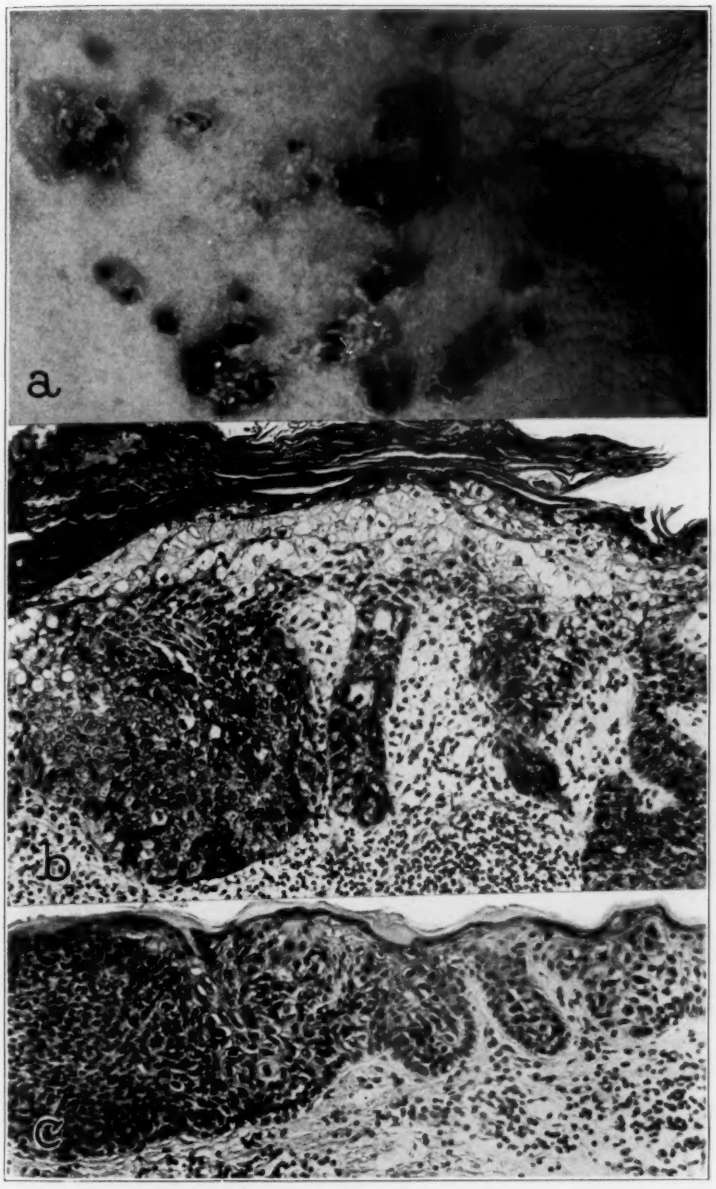

Fig. 3.—Case 5 clinically simulated Bowen's disease. *a*, the small, verrucous hard crusting lesions with rolled borders which are characteristic of the arsenical type of epithelioma. *b*, squamous cell epithelioma, grade 3, with numerous mitotic figures invading the cutis. There are verrucous crusting and a peculiar vacuolation of cells in the upper portions of the epidermis. *c*, section from a case that clinically was one of superficial epitheliomatosis and arsenical epithelioma. There is transition from basal cell epithelioma to squamous cell epithelioma, grade 1, in situ, simulating Bowen's disease.

skin adjacent thereto in some of the sections. A few crystals were present about the blood vessels in the upper part of the cutis. Urinalysis revealed 0.22 mg. of arsenic in 620 cc. of urine. After four injections of sodium thiosulphate an examination of the urine for arsenic gave negative results. All of the epitheliomas were excised or cauterized, and the larger lesion on the scalp was given postoperative treatment with radium.

On questioning, the patient admitted having taken ascatco, each fluid ounce of which, according to the label, contains 1.96 grains (about 0.12 Gm.) of opium and the maximal dose of which contains 0.11 grains (about 0.0066 Gm.) of arsenous acid. The patient had taken the medicine thirty years before for asthma, using four bottles each of a capacity of 5 ounces (150 cc.) in a year. The patient said that he had never taken any other medicine containing arsenic. It appears, therefore, that it took about twenty years for arsenical keratosis and epitheliomas to develop after the patient stopped taking the medicine.

Two months later another lesion on the back, also a squamous cell epithelioma, was removed. Arsenic was again demonstrated by Osborne's method, and direct chemical analysis disclosed 0.086 mg. of arsenic in each gram of tissue. An examinaton of a specimen of hair for arsenic gave negative results.

Case 5.—A woman, aged 44, had a lesion in the right axilla for fifteen years (fig. 3*a*). Presumably she had taken solution of potassium arsenite for St. Vitus' dance when she was 14 years of age, in a dose of from 3 to 16 drops three times a day for more than a year. The arciform arrangement of the lesions and their crusting simulated the picture of Bowen's disease. A specimen for biopsy, taken from the upper pole of the lesion, revealed a squamous cell epithelioma, grade 3, in situ, and by Osborne's method numerous crystals of arsenic were demonstrated in the epidermis and cutis; they were more numerous where epitheliomatous changes were occurring. Direct chemical analysis revealed 0.0018 mg. of arsenic per gram of tumor tissue. An examination of a specimen of hair for arsenic gave negative results. Further histologic studies disclosed squamous cell epithelioma both in situ and invading the tissue, varying from grade 1 to grade 3 (fig. 3*b*). There was little of the clumping of cells that is seen in Bowen's disease.

BOWEN'S DISEASE

I adhere to the concept of Bowen's disease as given in his original description.[13] In many cases of senile keratosis, and keratosis caused by roentgen rays, tar and arsenic the histopathologic picture is similar to, or even indistinguishable from, that of Bowen's disease.[14] These are potentially malignant conditions, eventually developing into penetrating epitheliomas in 20 per cent or more of the cases. The designation of these conditions as precancerous dermatosis has been supported recently by Bloch.[15] Histologically the tumors are epitheliomas in situ. When the basal cell layer is broken, frank squamous cell epithelioma is present, and the tumor should not then be designated as being of

13. Bowen, J. T.: Precancerous Dermatoses: A Study of Two Cases of Chronic Atypical Epithelial Proliferation, J. Cutan. Dis. **30**:241 (May) 1912.

14. Montgomery, Hamilton, and Dörffel, Julius: Verruca senilis und Keratoma senile, Arch. f. Dermat. u. Syph. **166**:286, 1932.

15. Bloch, Bruno: Cancers and Precancerous Affections from the Dermatological Viewpoint, Cancer Rev. **7**:65 (Feb.) 1932.

the Bowen type of epithelioma. Some ordinary squamous cell epitheliomas of the mucous membranes and other tissues present the histologic features of Bowen's disease without presenting the clinical features of solitary lesions with arciform configuration or of multiple lenticular plaques. Anderson [16] has suggested that Bowen's disease is the result of the ingestion of arsenic. In his case 1, the evidence he presented supports the diagnosis of the arsenical type of epithelioma with arsenical keratosis rather than that of Bowen's disease. In none of the reports of true cases of Bowen's disease in the literature is there mention of arsenical keratosis or of pigmentation, and Fraser's [17] case is the only one in which there was a history of the ingestion of arsenic.

Five cases fulfilling the clinical and histopathologic requirements of Bowen's disease have been seen at the clinic. In none of these was it possible to obtain a history of the ingestion of arsenic, and in none was there evidence of arsenical keratosis or of pigmentation. In three of the cases there was already evidence of a break in the continuity of the basal cell layer; in none of the sections was there any evidence of a relation of histologic changes to altered sweat ducts. In three there was a single lesion; in one there were two superficial lesions on the thigh, and in another there was a lenticular plaque on each arm resembling the lesion of superficial epitheliomatosis. In one case a solitary lesion on the leg resembling a nodulo-ulcerative sphiloderm had been present for thirty years without progression; histologically there was no evidence of a break in the continuity of the basal cell layer. In all but one case the lesions were excised; in that one treatment with radium and roentgen rays was given elsewhere. All lesions have remained healed for from one to eleven years. Chemical studies for arsenic were not made on any patients in this group.

SUPERFICIAL EPITHELIOMATOSIS

I wish to report the results of the study of forty-one cases of superficial epitheliomatosis, including the first series of eighteen cases previously reported.[18] The individual lesions are characterized by the fine, threadlike, rolled, pearly borders and relative lack of induration; in the dry form, which predominates, the histologic picture usually is that of basal cell epithelioma, whereas in the moist, eczematoid type

16. Anderson, N. P.: Bowen's Precancerous Dermatosis and Multiple Benign Superficial Epithelioma: Evidence of Arsenic as an Etiologic Agent, Arch. Dermat. & Syph. **26**:1052 (Dec.) 1932. Ayers, Samuel, Jr., and Anderson, N. P.: Cutaneous Manifestations of Arsenic Poisoning, ibid. **30**:33 (July) 1934.

17. Fraser, J. F.: Bowen's Disease and Paget's Disease of the Nipple: Their Relation to Dyskeratosis, Arch. Dermat. & Syph. **18**:809 (Dec.) 1928.

18. Montgomery, Hamilton: Superficial Epitheliomatosis, Arch. Dermat. & Syph. **20**:339 (Sept.) 1929.

the picture is that of basal-squamous or squamous cell epithelioma, occasionally presenting changes similar to those seen in Bowen's disease, the latter in some instances possibly the result of previous radiotherapy. The literature and various phases of the disease are covered in articles by Ormsby,[19] Little,[20] Wise,[21] Fraser [17] and myself [18] and in recent publications by Rousset [22] and Beck.[23]

It was possible to follow up sixteen of the eighteen patients with superficial epitheliomatosis whose cases were previously reported.[18] Three of the patients are dead, though none because of epithelioma. In one case the so-called precursor lesions of superficial epitheliomatosis (the pearl-like nodules of Little) had developed into typical lesions of Recklinghausen's disease. In this case (case 1 of the previous paper) an adenocarcinoma of the breast developed at the site of the excision of a lesion of superficial epitheliomatosis; the wound had never completely closed. There was no evidence, clinically or histologically, of recurrence of the epithelioma. I have yet to identify a precursor lesion resulting in superficial epitheliomatosis. New lesions of epitheliomatosis developed subsequently in 56 per cent of the sixteen cases, in two of which there were histologic changes similar to those of Bowen's disease. A recurrence of the original lesions took place in one case after fulguration and in several others after treatment by radium or by roentgen rays, although two lesions were finally healed by radiotherapy. In one case, in which the lesion was histologically a basal cell epithelioma, no treatment was given, and the growth merely increased in size in the following ten years. There was no recurrence of any epitheliomas that were treated by excision or cautery from six to fifteen years later.

In the subsequent series of twenty-three cases of superficial epitheliomatosis, the data regarding age, duration, sex, multiplicity of lesions, type, histopathologic changes, associated dermatosis and ordinary epithelioma correspond so closely to those originally given that they need not be repeated. In one case in which histologic examination was not made metastasis and death apparently resulted. The relative resistance of superficial epitheliomatosis to treatment by roentgen rays or by radium was again seen, especially in one case in which the patient, aged

19. Ormsby, O. S.: A Practical Treatise on Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1927, p. 685 and 699.

20. Little, E. G. G.: Erythematoid Benign Epithelioma, Brit. J. Dermat. **35**: 435 (Dec.) 1923.

21. Wise, Fred: Multiple Superficial Benign Epithelioma of the Skin, Arch. Dermat. & Syph. **19**:1 (Jan.) 1929.

22. Rousset, J.: Les dyskeratinisations épithéliomateuses, Paris, Masson & Cie, 1931.

23. Beck, S. C.: Epitheliome, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, p. 208.

75, had a large plaque on the back with a fungating tumor in the center. Because of the patient's age and the presence of hypertension, intensive treatment with radium was given. Yet eight months later there was a massive recurrence of squamous cell epithelioma, grade 4, surrounded by an area of actinodermatitis. Following excision and skin grafts there has been no recurrence in two and a half years. Michelson's [24] case of a patient with lesions of superficial epitheliomatosis which recurred in areas of actinodermatitis and histologically were still basal cell epitheliomas is further evidence of the frequent ineffectiveness of radiotherapy against these lesions.

COMMENT

Anderson [16] has suggested that there is a probable relationship between Bowen's disease and multiple benign epithelioma (superficial epitheliomatosis) and that arsenic may be the etiologic agent of both conditions. With this view I cannot agree. It is true that the two conditions are found associated and that either can be associated with ordinary epithelioma or an arsenical type of epithelioma, but I believe that this is so because of a common but unknown factor which predisposes the skin of certain persons to the development of various types of epithelioma. The ingestion of, or exposure to, pentavalent or inorganic arsenic, which has an affinity for the epidermis, precipitates the formation of epithelioma of rather characteristic type when the unknown factor is present. I have shown that neither the amount of arsenic ingested nor the duration of treatment has a bearing on the formation of epithelioma and that one may find as large amounts of arsenic in the skin in many benign forms of dermatosis as are seen in keratosis or epithelioma of the arsenical type. In none of the forty-one cases of superficial epitheliomatosis was there any evidence of arsenical pigmentation or keratosis.

From the original series of eighteen cases of superficial epitheliomatosis, several other cases were excluded simply because of the presence of keratosis or pigmentation. Of sixteen of the original eighteen patients who were followed up, only one recalled having taken arsenic, but this patient stated that members of three generations in her family had had epitheliomas of the skin, so she did not think that arsenic was a factor. Her lesions, which histologically were basal cell epitheliomas, had not recurred eleven years after excision. The patient who had superficial epitheliomatosis and psoriasis independent thereof was a physician who gave a detailed history of previous medication without

24. Michelson, H. E.: Multicentric Benign Superficial Epitheliomas, Arch. Dermat & Syph. **25**:1134 (June) 1932.

mention of arsenic. In Ormsby's [25] case of superficial epitheliomatosis, with metastasis and death, there was no evidence of arsenical keratosis or pigmentation or of psoriasis when the patient was examined by Ormsby, nor was a history of medication with arsenic obtainable.

Determinations of arsenic were not made in the original series of cases of superficial epitheliomatosis. In one typical case in the subsequent series of twenty-three cases of superficial epitheliomatosis, the examination of the urine for arsenic gave negative results; in a second case there was a history of the ingestion of arsenic, but all the lesions of superficial epitheliomatosis examined were basal cell, and in a third and a fourth case, in which histologically the lesions were basal cell and basal-squamous cell epithelioma, respectively, arsenic crystals were revealed by Osborne's method in small but similar amounts both in the epithelioma and in the normal epidermis adjacent thereto. Direct chemical analysis for arsenic gave negative results, and there was no clinical evidence or history of the patient having been exposed to arsenic.

In a case encountered recently in which there was a solitary lesion of superficial epitheliomatosis of the face which clinically presented a fine, threadlike, rolled border, there were histologic changes of the type seen in Bowen's disease, which suggested senile keratosis as an etiologic factor. Studies for arsenic by Osborne's method and by Osterberg's method of direct chemical analysis failed to reveal evidence of arsenic in the epithelioma. Finally, I wish to cite the following case:

CASE 6.—A man, aged 50, as a child took solution of potassium arsenite for chorea. Numerous lesions of superficial epitheliomatosis, which histologically were basal cell and basal-squamous cell epithelioma, had been excised in 1930 and in 1934. Also, typical arsenical keratotic lesions of the palms and soles with a slight pigmentation of the trunk had been present. In 1934 biopsy of an atypical verrucous lesion revealed a squamous cell epithelioma, grade 2, in situ, with changes of the type seen in Bowen's disease, and examination by Osborne's method revealed more arsenic in the epithelioma than in the normal adjacent epidermis. On the other hand, a typical lesion of superficial epitheliomatosis, probably a basal cell epithelioma, was excised from the back, together with a separate piece of normal skin adjacent thereto. Direct chemical analysis revealed 0.0077 mg. of arsenic for each gram of normal skin as contrasted with 0.005 mg. of arsenic for each gram of epithelioma. Examinations of urine and hair for arsenic gave negative results. A patch test with potassium arsenite gave negative results on three occasions.

This case exemplifies how both conditions may be present; yet to interpret the lesions of superficial epitheliomatosis as being due to arsenic, or as being precipitated by it, is unwarranted since more arsenic was present in the adjacent normal skin than in the epithelioma.

25. Ormsby, O. S.: Personal communication to the author.

As has been stated, in seven of the sixteen cases of the arsenical type of epithelioma with arsenical keratosis there also were lesions of superficial epitheliomatosis. It would seem that Anderson's [16] cases 2 and 3 belong in this group. I believe that confusion exists when these two types of epithelioma appear in the same patient (fig. 3*c*). It is not always possible in such cases to be sure what part the arsenic plays in the development of epithelioma, especially of the basal cell type. The same holds true in cases of Bowen's disease, but here even clinical differential diagnosis may be impossible.

SUMMARY AND CONCLUSIONS

Superficial epitheliomas of the skin, presumably precipitated by the ingestion of arsenic, are described and differential diagnosis is given from lesions of superficial epitheliomatosis and of Bowen's disease. The clinical picture of Bowen's disease may be simulated by epithelioma of the arsenical type, and arsenical keratosis or pigmentation need not be present. Confusion arises when more than one type of epithelioma occurs in the same case. The absence of arsenic in the urine, hair or skin does not deny, any more than the demonstration of arsenic itself implies, that arsenic is an etiologic agent in the disease under consideration. It is necessary to weigh clinical, pathologic and chemical observations before deciding that arsenic is a factor in a given case. The reaction of the patient to the ingestion of pentavalent or inorganic forms of arsenic cannot be anticipated, nor can one determine whether keratosis, pigmentation, epithelioma or hepatic cirrhosis will develop or how long a time will elapse before the lesion will develop. Apparently there is a factor of individual sensitivity or idiosyncrasy to the pentavalent and inorganic forms of arsenic similar to that seen following treatment with arsphenamine (trivalent arsenic).

In 20 per cent of the cases of arsenical keratosis epithelioma of the arsenical type was present associated with keratosis or epithelioma independent of keratosis. In 11 per cent of the cases of arsenical keratosis there was superficial epithelioma of the arsenical type on the trunk. Arsenical keratosis, therefore, must be regarded as potentially malignant and hence should be included among the precancerous types of dermatosis. Epitheliomas precipitated by arsenic are usually squamous cell epitheliomas, often with microscopic features simulating Bowen's disease, but usually of malignancy graded 2 or 3, although they may not clinically run as malignant a course as ordinary squamous cell epitheliomas graded 2 or 3. Further studies of the series of cases of superficial epitheliomatosis confirm the impression that this is a relatively benign disorder, usually running a relatively benign course, as compared with ordinary basal cell epithelioma. The treatment of choice is surgical excision or excision by cautery for all the conditions mentioned. The lesions are prone to recur following radiotherapy.

ABSTRACT OF DISCUSSION

DR. EARL D. OSBORNE, Buffalo: Most of the members are aware of the paper by Muir and Tannenholz which appeared in the *Archives of Pathology* last year. On the basis of their work with egg albumin and rat tissues, the authors were satisfied that what I thought was arsenic trisulphide was, in their opinion, a sulphide of albumin. If their view is correct, the work which my associates and I have done on arsenic in the tissues is of very little value. I do not believe that this is the case, and a number of other men throughout the country, using our methods, are of the same opinion. From Dr. Montgomery's data it is evident that our method compares favorably with Osterberg's modification of the Gutzeit method for the determination of arsenic. I should like to ask Dr. Montgomery how large a series of parallel observations he has with Osterberg's method and our method, and also how the two methods check in tests on the skin of normal persons with no history of the ingestion of arsenic and on normal skin adjacent to areas of arsenical keratosis.

Regarding the controls which we used in perfecting our method, I wish to point out that numerous chemists have agreed that arsenic, if present in the tissues, must appear as arsenic trisulphide under the conditions of our method. Any one wishing to verify this can take any form of arsenical solution and subject it to the same conditions that are used in the method of preparing the tissue, and arsenic trisulphide will result.

Any one who contemplates using this method should become well acquainted with the microscopic appearance of pure arsenic trisulphide crystals. Arsenic trisulphide crystals are not brown but are pale green or greenish yellow with a definite halo. Furthermore, the crystals are nearly always of uniform size and, from what I can determine, are somewhat smaller than the crystals described by Muir and Tannenholz.

We have seen hundreds of sections of skin prepared for analysis for arsenic that were entirely lacking in any crystals simulating arsenic trisulphide. If Muir and Tannenholz are correct, we should find albuminous sulphide present in every section prepared by this method.

Regarding our controls, we used every possible kind of control when we first presented our work. We first studied arsenical keratosis and pigmentation. Our controls were entirely normal human skin and rabbit skin. In view of the work of Muir and Tannenholz, we should have used animal liver and kidney tissue free from arsenic as controls as well as egg albumin. This work is being carried on, and we hope to report later.

DR. FRANCIS J. EICHENLAUB, Washington: I wish to show three slides in connection with a case of Bowen's disease. In one instance Bowen's disease can be seen clearly on both sides, with a typical prickle cell carcinoma in the center. I report this briefly, for it is the only case of which I know of a prickle cell cancer in the center of a typical lesion of Bowen's disease.

DR. GEORGE M. MACKEE, New York: Dr. Montgomery has studied his material exhaustively from a scientific standpoint, and the lesions were definitely due to arsenic. I understand that all the lesions were of the squamous cell type. I think that I have seen basal cell epitheliomas develop in arsenical keratoses and in the apparently normal skin of arsenical patients. However, I was unable to prove that arsenic was the cause. In the vast majority of cases the lesions have been of the squamous cell type. Has Dr. Montgomery seen any basal cell epithelioma that he thought was caused by arsenic? Dr. Gaul, of my clinic, is doing a great deal of biospectrometric estimation of metals in the skin. Most of the work has been in connection with lead, copper and nickel. Heavy deposits of lead and

copper have been found in the skin of patients with neurodermatitis disseminata and deposits of nickel in the skin of patients with psoriasis. He has just begun the study of arsenical retention. He has not gotten far, but his results do not correspond with most of the reports based on the chemical analysis of the blood, the urine and the skin.

Dr. Isadore Rosen, New York: I was very much interested in Dr. Montgomery's paper and feel that because of the time limit he could not emphasize all the salient features of the subject. I should like to know whether he has compared the effect of trivalent and pentavalent arsenic in the development of epithelioma. It has been my experience in syphilitic lesions of the mouth, especially in leukoplakia associated with ulcerating glossitis, that trivalent arsenic has in a number of cases stimulated epithelial proliferation and led to the development of a malignant process.

To illustrate the rapidity with which trivalent arsenic may act, I wish to report the following interesting case seen in the clinic with which I am associated. A man, aged 40, had an ulcerated lesion of the lower lip the size of a small hazelnut which had been present for about seven weeks and which looked like a primary lesion. Repeated dark-field examination failed to reveal spirochetes, but the Wassermann reaction was positive. On the strength of this we treated the patient with arsphenamine, and to our surprise, instead of responding, within two weeks the lesion increased to twice its size on admission. This made us suspicious, and histologic examination revealed a squamous cell carcinoma. There is a great divergence of opinion among syphilologists regarding the treatment of syphilitic leukoplakia with arsphenamine. I feel that they should not be used in the treatment of long-standing extensive leukoplakia. I recall several cases in which the treatment with arsphenamine of men between the ages of 60 and 65 was followed by the development of epithelioma of the oral mucosa.

Dr. Karl G. Zwick, Cincinnati: The title and résumé of Dr. Montgomery's paper indicate that it is possible "to differentiate superficial epitheliomas of the trunk and extremities of the arsenical type from true cases of superficial epitheliomatosis and Bowen's disease." Without going into detail, I note that the feasibility of such a differentiation should be borne in mind in connection with litigations involving the etiology of an epithelioma. Arsenic is, of course, ingested, practically speaking, continually, and its nearly ubiquitary presence can be shown spectrographically.

If I understood Dr. Montgomery correctly, he shares the opinion that the valency of the arsenic decides or at least influences the cancerigenic quality of an arsenical compound. I wonder whether he would, in view of this, go so far as to suggest or to urge—for instance, in the treatment of syphilis—the use of one arsenical in preference to, or to the exclusion of, another.

Dr. E. J. Trow, Toronto: I should like to ask Dr. Montgomery's opinion of a case. A man, 50 years of age, for two or three years had been taking a cure for "fits" containing solution of potassium arsenite, when there developed an epitheliomatous change of a prickle cell type over the trunk and the back. On the palms, however, typical arsenical keratosis developed, and over the backs of the fingers the lesions were greatly elevated and showed epitheliomatous change. This patient seemed to present two varieties of degenerative change from the same cause. Could the influence of light explain the greater reaction on the hands?

Dr. A. Benson Cannon, New York: My associates and I have observed multiple basal cell epitheliomas in several patients with syphilis who gave a history of having received many injections of arsphenamine a number of years previous to the appearance of the epitheliomas. This has led us to examine for arsenic

the blood, urine and skin of other patients suffering with epitheliomas, and we have found in the great majority of cases that the patients with multiple basal cell epitheliomas give a history of having received arsenic in some form or have a large quantity of arsenic in specimens of the blood, urine and skin. Another type of basal cell epithelioma that might be considered as possibly related in some way to arsenic is the type seen in comparatively young persons in the form of an epithelioma recurring in different locations on the face at intervals of several years. In these patients we have demonstrated the presence of large quantities of arsenic both by chemical analysis and by the observation of crystals in histologic sections of the skin. We find it difficult to evaluate the presence of arsenic in large quantities as demonstrated in the blood, urine and skin because of the varied pathologic conditions in which it is found in excess. I think that before we can ascribe any disease to arsenic we must know more about the significance of the metal in normal persons. Dr. Montgomery's paper is a most interesting and timely discussion of the subject.

DR. HAMILTON MONTGOMERY, Rochester, Minn: In answer to Dr. Osborne's question regarding the arsenic content of normal skin in various cases of benign dermatosis, studies were made of both normal and pathologic areas by the direct method of chemical analysis (Osterberg) and by Osborne's method of microchemical analysis. In three cases no arsenic was demonstrated by either method in the normal or pathologic areas. In nine cases, however, arsenic was demonstrable by both methods in varying amounts, and none of the patients gave signs of arsenical pigmentation, arsenical keratosis or epithelioma. It was not possible to obtain a history of ingestion of, or of exposure to, arsenic in all of these cases.

Answers to several of the questions are to be found in the reports of illustrative cases given in the paper.

In answer to the question of whether arsenic can cause basal cell epithelioma, I will say that I think that it probably can, just as in occasional instances basal cell epithelioma may arise as a sequel to senile keratosis. Both arsenical and senile keratosis, however, usually show various phenomena of malignant dyskeratosis and changes characteristic of Bowen's disease, eventuating in squamous cell epithelioma, grade 2 or grade 3. The mere demonstration of arsenic in the tissues is not enough to enable one to say that arsenic is an etiologic factor, nor is it possible to prognosticate the course of the arsenical type of epithelioma on the basis of histologic grading. It is probable that an individual idiosyncrasy exists similar to that seen in reactions to arsphenamine. I do not believe that actinic rays are of primary significance in the development of arsenical keratosis or epithelioma.

With regard to the points raised by Dr. Eichenlaub, I can say that I have seen three cases of Bowen's disease in which the basal cell layer was broken through and frank, invading squamous cell epithelioma developed.

None of the patients in my series had leukoplakia. Theoretically it is possible that arsenic in trivalent form can stimulate epitheliomatous changes.

FOLLICULITIS BARBAE TRAUMATICA

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The term sycosis vulgaris, as a perusal of the recent textbooks on dermatology indicates, is now used exclusively for a kind of primary coccogenous purulent folliculitis of the regions of the beard and mustache. Stellwagon and Gaskill [1] stated: "As the disease [sycosis vulgaris] is now known to be microbic in origin, the term 'non-parasitic,' formerly used to distinguish it from parasitic [that is, tineal] sycosis . . . is no longer applicable." Thus both tineal sycosis and coccogenous sycosis are primary parasitic infections of the hair follicles. There appears, however, to be a form of folliculitis barbae which is truly nonparasitic primarily, although it may become so secondarily, and which deserves description apart from the true parasitic types of folliculitis of the beard. There is some similarity between this form and that classified as a form of sycosis vulgaris by Walker.[2] He described a rare form of sycosis occurring in persons with very heavy beards. A number of pustules are present, usually under the chin, and when these are closely examined each is seen to surround a hair, of which the free end has not escaped from the skin but is growing downward as it lengthens and thus producing irritation. With a little effort the buried end may be disinterred, and the pustule disappears. Sutton [3] classified the condition "ingrowing hair" under keratosis pilaris. All the clinical evidence is against such a classification; besides, the one is a spontaneous condition, and the other is induced.

"Ingrowing hair" occurs only in the area of the beard in men and is associated with shaving, particularly with shaving "against the grain." It is a well known although minor clinical condition. For the average white man it is only an occasional complication. It is generally believed to be the result of mechanical alteration of the direction the hair normally should pursue. In the white man an "ingrowing hair" is commonly seen in the form of one or two inflammatory papules requiring

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1. Stellwagon, H. W., and Gaskill, H. K.: Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1921, p. 1063.

2. Walker, Norman: Introduction to Dermatology, ed. 8, New York, William Wood & Company, 1925, p. 219.

3. Sutton, R. L.: Diseases of the Skin, ed. 8, St. Louis, C. V. Mosby Company, 1931, p. 509.

perhaps from two to four weeks for resolution through absorption or mechanical removal of that part of the hair involved.

As is well known, the lesion is a red, sometimes painful but always uncomfortable, papule between the size of a pinhead and that of a split pea and resembling in appearance a lesion in an early stage of acne. However, it does not go on to suppuration, or if it does, the amount of pus is infinitesimal. The lesions persist for a variable period but when teased apart they reveal curled-up hairs.

For many years there has been observed in the large clinic for Negroes of the Graduate Hospital and more recently in the clinic for patients with syphilis at the Philadelphia General Hospital a chronic, papular, sometimes pustular condition of the orifices of the hair follicles of the bearded region, which superficially simulates ordinary sycosis vulgaris. On close inspection and on microscopic study a lesion not infected secondarily is found to be different clinically and histologically from the ordinary types of sycosis vulgaris. It occurs almost exclusively in the bearded region below the chin and jawbones. I have never seen it in the area of the mustache. I believe that most dermatologists who have any contact with a clinic for Negroes certainly have observed this condition.

Fibroid change, accounting for some of the keloid-like growths, can easily be detected clinically in many of the papules and confirmed by histologic examination. This fibroid condition is doubtless the result of both the chronic irritation and the inherent susceptibility of the skin of the Negro to sclerosis.

Subjectively there is no pain or itching but merely disfigurement, which is often marked. Only in exceptional instances has a patient with this condition actually come to the clinic with that as his chief complaint, but commonly it is observed in the course of the routine examination to discover the cause of another complaint.

This condition, like coccogenous sycosis, always develops after puberty. Forty-five of 87 persons examined by Dr. Stein one after the other as they came to the clinic for patients with syphilis at the Philadelphia General Hospital and 199 of 338 Negroes at the New Jersey State Prison in Trenton examined by Dr. Schildkraut presented this form of folliculitis in varying degrees.

The diagnosis is not difficult. In the Negro the chronic, papular, grossly noninflammatory eruption limited to the bearded region is characteristic. The inflammatory appearance of the skin between the pustules present in true sycosis is absent in this condition, as is central piercing of the lesion by a hair. In this condition tearing a papule apart will often reveal the hair within the papule. Pustules are not common in traumatic folliculitis of the beard, and crusting is never seen except over an

occasional lesion previously the seat of a secondary infection which has undergone pustulation. The lesions in this condition are isolated, and confluent areas commonly seen in coccogenous sycosis are never observed. There are no acute exacerbations as in coccogenous sycosis; the lesions are generally of many years' standing and of sluggish character.

In coccogenous sycosis the hairs are visible, projecting up through the center of the inflamed lesion; in traumatic folliculitis no hairs are visible until careful tearing apart of the lesion with a needle or a fine pointed instrument reveals the hair more or less encased within the papule.

Fig. 1.—Photograph showing the usual site of lesions on the bearded area, particularly below the inferior maxilla.

Shaving improves coccogenous sycosis vulgaris but makes this condition worse. The disease is readily differentiated from simple acne vulgaris. It must also be differentiated from the type of traumatic folliculitis seen after close shaving, especially with a dull razor, in which one finds red, painful, tender papules varying from the size of a pinpoint to slightly larger, which clear up in from twenty-four to forty-eight hours if the patient does not shave or does so lightly with a sharp razor. The latter condition is really a superficial traumatic folliculitis in which the direction of the hair has not been altered, but merely the follicular orifices have been injured. This condition is particularly common in the white man who shaves daily, closely and with a dull razor.

The following description of the histologic findings is based on the microscopic examination of serial sections of several large papules removed from the neck of the patient whose photograph is shown in figure 1 and from several others. The papule consists of edematous tissue infiltrated with cells. The cells surround the hair follicle, which itself appears enlarged and contains normal and what appears to be abnormal degenerated hair (fig. 2). The inner wall of the follicle presents a definite degree of keratosis whereas the surrounding tissue,

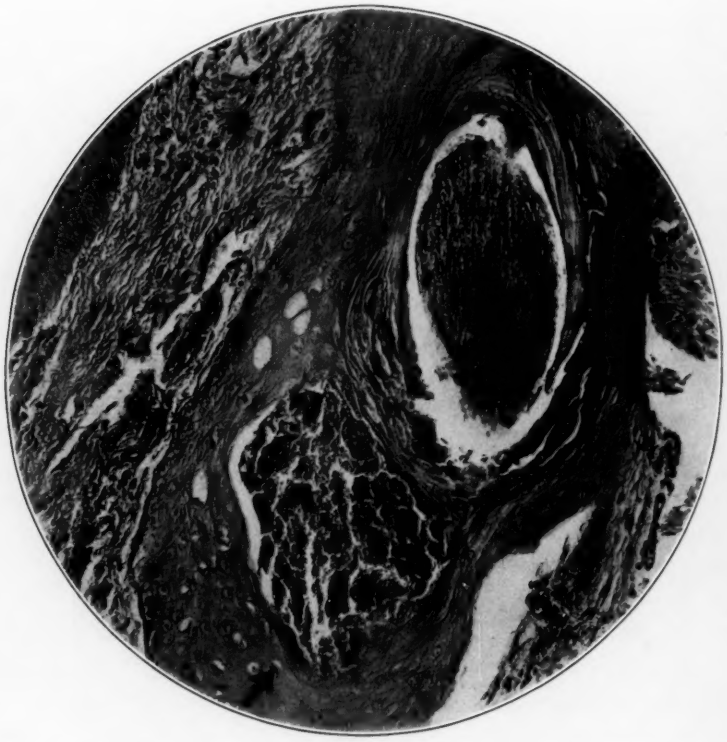

Fig. 2.—Photomicrograph of the lesion as a whole (high power, dry lens; × 128). Note the bodies within the hair follicle and the perifollicular reaction. In the lower part of the field are a number of giant cells in the protoplasm of which are many pigment granules. The light-colored mass in the hair follicle is the normal hair shaft; the dark mass is presumably degenerated hair.

in some sections at least, shows some fibrosis, probably the result of inherent tendencies on the part of the skin of the Negro to react in this manner to injuries, mechanical or otherwise.

The essential process appears to be a perifolliculitis due to a foreign body in the follicular epidermis. There are, besides what appears to be degenerating hair in the follicular epidermis and alongside the normal

hair in its follicular space, collections of lymphocytes and mast cells with foreign body giant cells containing pigment granules (from the degenerating hair?). The reaction is limited to the upper reaches of the perifollicular area, but there appears to be an abnormal collection of corneous material lining the follicular cavity. In a word, the surrounding area of inflammation consists of loosened connective tissue

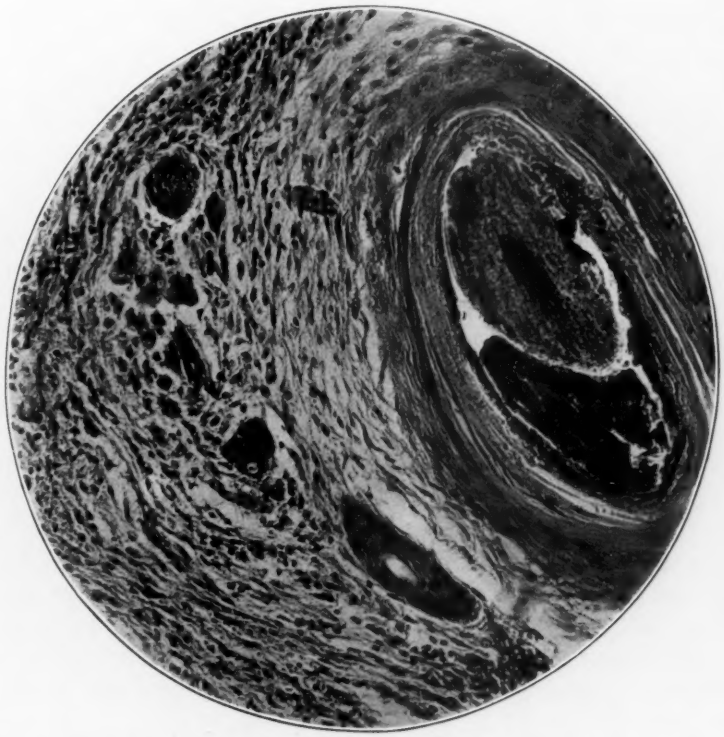

Fig. 3.—Photomicrograph (high power, dry lens; × 128), showing the intra-epidermal location (the arrow indicates the site) at certain levels of the dark mass (misdirected hair?) and the degenerated character of the intra-epidermal mass.

having an edematous character with some fibrous changes analogous to those in granulation tissue. Polymorphonuclear leukocytes, organisms and any elements suggestive of a pyogenic reaction are absent. In none of the sections examined was it found that hair papillae or hair follicles had been destroyed.

MERCURY INUNCTIONS

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WITH THE COLLABORATION OF

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INFLUENCE OF THE VEHICLE ON ABSORPTION

In our previous papers on inunctions the excretion and absorption of mercury after simple and those after clean inunctions have been compared,[1] and the advantage of massive weekly inunctions has been demonstrated.[2] In the first article of the present series[3] the relation of the concentration of the mercury in the ointment to absorption and excretion has been shown. The function of the oleate and the effect of the size of the particles as found in ointment of colloidal mercury was discussed, while the relation of the vehicle to the absorption of mercury with a petroxolin base was only touched on. It appeared desirable to make a more extensive investigation of this subject since the vehicles of the mercurial ointments of the various pharmacopeias differ considerably, partly in the emulsifiers which are used to extinguish the mercury and partly in the fats of the ointment. So far as these variations were not fanciful they were introduced chiefly for pharmaceutic reasons—for convenience in preparation or to secure the consistency

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This group of papers concludes the investigations on this subject which were carried on through a number of years under grants from the Committee on Research in Syphilis, from the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association and from the United States Pharmacopeia Committee of Revision.

1. Cole, H. N.; Gammel, J. A.; Rauschkolb, J. E.; Schreiber, N. E., and Sollmann, Torald: Clinical Excretions of Mercury, Arch. Dermat. & Syph. **17**: 625 (May) 1928.

2. Cole, H. N.; Rauschkolb, J. E.; Schreiber, N. E., and Sollmann, T.: Massive Weekly Inunctions with Mercury, Arch. Dermat. & Syph. **20**:176 (Aug.) 1929.

3. Cole, H. N.; Schreiber, N. E., and Sollmann, T.: Mercurial Ointments in the Treatment of Syphilis, Arch. Dermat. & Syph. **21**:372 (March) 1930.

that appealed to the devisor of the formula. It is conceivable that these differences might tend to favor or hinder the penetration of the ointment directly or by facilitating or impeding friction. These matters could be decided only by trial, and the differences in the degree of absorption of the mercury from the various bases should be discernible by studies of excretion.

Wild and Roberts [4] have attempted to investigate this problem of the influence of the vehicle on the absorption of mercurial ointments by rubbing them into the skin under uniform conditions and weighing the unabsorbed ointment which could be scraped off with a dull razor blade. This method could not give any direct information concerning the absorption of the mercury; but even as regards the penetration of the ointment it does not give reliable information, since the amount of ointment which can be scraped from a surface depends not only on the amount present but on the consistency and adhesiveness of the ointment.

In the present paper the data on the relation of the vehicle to the absorption have been extended to a series of bases: oil of theobroma, anhydrous wool fat and vanishing cream (obtained through Chairman Fullerton E. Cook of the U. S. P. Committee of Revision) and a soft ointment base.

MATERIALS AND TESTS

With these series of inunctions the following procedure was adopted: Each ointment was used generally on six patients selected from the Cleveland City Hospital, 4 Gm. of the ointment being rubbed into the skin by the patient each day for twenty-eight days. Each inunction lasted thirty minutes, except that with the vanishing cream preparation it was found that after ten minutes of inunction the cream was rubbed in. The regions of the body were used in rotation in the usual manner. The excretions were collected, generally for three days each week, followed by an intermission of four days. The three day specimens were then combined for analysis. For a two day period preceding the test the urine and feces were analyzed to establish the absence of mercury, and for a three day period one week after the termination of the course of treatment they were analyzed to study the decline of the excretion. The estimations of mercury were made by the method of Schreiber, Sollmann and Booth.[5]

Composition of the Ointment Bases.—The base of the U. S. P. 50 per cent stronger mercurial ointment, which may be taken as the norm, consists of equal parts of suet and benzoinated lard; oleate of mercury is used as an emulsifying agent in the ratio of 2 per cent of the finished ointment.

The soft ointment base consists of one-third suet and two-thirds benzoinated lard; oleate of mercury is used as emulsifying agent in the ratio of 2 per cent of the finished ointment. It is considerably softer than the official ointment and is accordingly somewhat easier to apply, but in time the mercury tends to settle

4. Wild, R. B., and Roberts, Ivy: Absorption of Mercurials from Ointments Applied to the Skin, Brit. M. J. **1**:1076 (June 26), 1926.

5. Schreiber, N. E.; Sollmann, T. and Booth, H. S.: The Determination of Traces of Mercury, J. A. Chem. Soc. **50**:1620, 1928.

out, so that the content becomes variable. A number of patients applied this preparation before the cause of error was appreciated. The observations on these patients were discarded. Precaution was then taken to prevent settling by keeping the ointment solidified in the refrigerator. All the results that are included are from this second series.

The ointment of oil of theobroma consists of oil of theobroma with mercury oleate used as emulsifier in the ratio of 2 per cent of the finished ointment. It is a soft solid at room temperature but melts on inunction.

The anhydrous wool fat base consists of four-fifths wool fat and one-fifth suet, with oleate of mercury as emulsifier in the ratio of 2 per cent of the finished product. The ointment is very stiff.

The petroxolin base consists of approximately equal quantities of white wax, light liquid petrolatum and ammonium oleate soap. This introduces the soap principle of suspension which is further utilized in the vanishing cream. Mercury oleate in the ratio of 2 per cent of the finished product is added as emulsifier. The ointment is rather soft.

The vanishing cream base consists of approximately 25 per cent stearic acid suspended in a watery potassium oleate soap. The ointment is made with 25 per cent of mercury (in contrast to the 50 per cent mercury used in all the preceding ointments), 5 per cent of mercury oleate, 5 per cent of wool fat and 65 per cent of vanishing cream. The ointment is white and, in contrast to the other preparations, leaves no bluish stain on the skin after inunction. The preparation does not spread readily on being rubbed into the skin, yet after eight to ten minutes of vigorous rubbing no more ointment is perceptible and the skin is no longer greasy. The point may well be raised that it would be more difficult to detect the ointment on the skin because of lack of color. Nevertheless, as we shall show later in the paper, the preparation must have been rubbed into the pores of the skin, for there was a urinary excretion comparable to that noted in the persons who used the other 25 per cent mercury ointments, indicating absorption into the blood stream from the hair follicles.

The base of the 25 per cent U. S. P. mercurial ointment consists of one part of yellow wax and four parts of benzoinated lard. The 50 per cent U. S. P. ointment is diluted with one third of this ointment base and one third of petrolatum.

RESULTS

Tables 1 and 2 give the data for the different vehicles as medians and extremes, indicating the daily level of excretion at the end of each week and the total or cumulative excretion to the end of the fourth week. The last is the most valuable datum, since it sums up all the other values. The data for the individual patients with each ointment were plotted graphically but are not reproduced in order to economize on space.

Urinary Excretion of Mercury.—The median cumulative excretion at the end of twenty-eight days (last column of table 1) had the narrow range of from 10.2 to 11.9 mg. of mercury for all the 50 per cent ointments; i. e., the extreme variation of the medians of the different ointments was less than ± 8 per cent of the central value for the whole series. This was far within the limits of accidental variation and therefore insignificant. The median daily excretion at the end of the fourth

week ranged from 0.74 to 0.9 mg. of mercury, a ± variation of 0.08 mg., or 10 per cent, which was also within the limits of accidental variations. At the end of the second week the range was from 0.26 to 0.38 mg., or a variation of ± 19 per cent, and in the first week from 0.11 to 0.26 mg., or 40 per cent; but in view of the increase in analytic error with small amounts of mercury this variation was also insignificant. The daily excretion in the first week of the period following the tests ranged rather more widely, with medians of from 0.24 to 0.73 mg., or a variation of ± 50 per cent from the central value, but we doubt

TABLE 1.—*Urinary Excretion of Mercury*

Ointment	Daily Level, Mg. End of Third and Fourth Days	End of First Week	End of Second Week	End of Third Week	End of Fourth Week	First Week After Use	Cumulative, 28 Days
50% Mercury Ointments							
U. S. P.	....	0.12 (0.02 to 0.40)	0.33 (0.15 to 0.7)	0.58 (0.31 to 1.77)	0.83 (0.38 to 3)	0.73 (0.65 to 1.30)	10.7
Soft ointment base	0.05 (0.03 to 0.1)	0.26 (0.08 to 0.58)	0.33 (0.13 to 1.11)	0.49 (0.09 to 0.91)	0.84 (0.10 to 2.45)	0.49 (0.08 to 1.89)	10.2
Oil of theobroma	0.09 (0 to 0.16)	0.15 (0.06 to 0.47)	0.26 (0.12 to 0.46)	0.79 (0.47 to 0.89)	0.86 (0.29 to 1.86)	0.24 (0.13 to 0.56)	11.6
Anhydrous wool fat	0.05 (0.01 to 0.09)	0.11 (0.01 to 0.45)	0.34 (0.09 to 1.56)	0.86 (0.17 to 2.37)	0.74 (0.22 to 2.15)	0.43 (0.12 to 1.71)	11.5
Petroxolin	0.06 (0.02 to 0.31)	0.21 (0.06 to 0.34)	0.38 (0.1 to 1.4)	0.71 (0.15 to 1.5)	0.90 (0.18 to 1.58)	0.38 (0.08 to 0.62)	11.9
25% Mercury Ointments							
U. S. P.	....	0.12 (0.04 to 0.47)	0.28 (0.06 to 1.10)	0.43 (0.06 to 1.11)	0.46 (0.08 to 1.47)	....	7.5
Vanishing cream*	....	0.13 (0.02 to 0.41)	0.21 (0.05 to 0.79)	(0.36 and 0.49)	(1.04 and 1.32)	(0.10 and 1.08)	

* There were two patients in this group.

whether this had any real significance as against the uniformity during the active period of inunction.

During the first two weeks the excretion after inunction of the 25 per cent ointment in vanishing cream was the same as that following the inunction of 25 per cent ointment with the U. S. P. base. Tests on four of the patients were dropped at that time because of salivation, and the remaining two patients made too small a number for drawing medians. However, the close concordance during the earlier weeks justifies the conclusion that there was no significant difference from the official ointment.

It appears, therefore, that the vehicles of the ointments do not influence the urinary excretion.

Fecal Excretion of Mercury.—The cumulative excretion (last column of table 2) showed much greater differences than the urinary excretion, the medians for the 50 per cent ointments ranging from 5.2 to 19 mg., i. e., a variation of ± 58 per cent from the central value. This appeared too great to be accidental. The descending order of magnitude of fecal excretion according to the base was: oil of theobroma, >U. S. P.> soft ointment base and petroxolin > wool fat. This order held also for

TABLE 2.—*Fecal Excretion of Mercury*

Ointment	Daily Level, Mg.						Cumulative, 28 Days
	End of Third and Fourth Days	End of First Week	End of Second Week	End of Third Week	End of Fourth Week	First Week After Use	
50% Mercury Ointments							
U. S. P.	....	0.35 (0.02 to 0.72)	0.48 (0.30 to 1.25)	0.44 (0.18 to 0.91)	0.45 (0.18 to 1.30)	0.45 (0.37 to 0.78)	13.5
Soft ointment base	0.06 (0.02 to 0.67)	0.25 (0.14 to 1.6)	0.45 (0.21 to 3.3)	0.32 (0.29 to 0.9)	0.40 (0.23 to 0.65)	0.53 (0.07 to 1.43)	8.3
Oil of theobroma	0.28 (0.02 to 0.98)	0.29 (0.12 to 1.48)	0.76 (0.42 to 1.3)	0.98 (0.69 to 1.26)	1.31 (0.07 to 1.5)	0.18 (0.09 to 0.45)	19.0
Anhydrous wool fat	0.04 (0 to 0.14)	0.16 (0.02 to 0.31)	0.23 (0.08 to 0.5)	0.25 (0.13 to 0.39)	0.22 (0.17 to 0.45)	0.16 (0.11 to 0.3)	5.2
Petroxolin	0.06 (0 to 0.33)	0.13 (0.06 to 0.31)	0.37 (0.16 to 0.41)	0.33 (0.23 to 0.69)	0.41 (0.07 to 0.84)	0.30 (0.1 to 0.84)	7.2
25% Mercury Ointments							
U. S. P.	....	0.15 (0.04 to 0.54)	0.27 (0.07 to 0.67)	0.33 (0.08 to 1.52)	0.43 (0.12 to 0.74)	....	6.8
Vanishing cream*	....	0.13 (0.04 to 0.36)	0.12 (0.09 to 0.30)	(0.10 and 0.14)	(0.31 and 0.39)	(0.15 and 0.45)	

* There were two patients in this group.

the weekly results in individual patients except in the first week, when the irregularities of defecation would have a relatively large share in the results. The uniformity of the urinary excretion indicates that the differences in the fecal excretion were not due to differences in absorption. They must have been due to the amount of ointment that was accidentally conveyed to the mouth by the hands and swallowed. This consorts with the taste and physical properties of the ointments: The ointment with a base of oil of theobroma, which caused the highest excretion, would be most likely to be swallowed because its taste is least offensive, and, conversely, the ointment with a base of wool fat, which caused the lowest fecal excretion, has a repulsive, rancid taste

which would serve as a warning. This explanation was confirmed by the fact that the difference between these two ointments disappeared completely a week after the inunctions were stopped, i. e., when they were no longer carried to the mouth.

The ointments with a petroxolin and with a soft base had lower values than the official ointment, probably because their thinner consistency allowed a thinner layer to be left on the hand.

Salivation.—This was very unevenly distributed in the series, as is shown in table 3. There was no correlation with the reported condition of the teeth; however, the report may not have stressed alveolar infec-

TABLE 3.—*Incidence of Salivation in Persons Receiving Mercurial Inunctions*

Ointment	Number of Patients	Patients Without Salivation	Patients With Salivation	Day of Onset
U. S. P., 50 per cent	10	8	2	13, 27
Soft ointment base, 50 per cent	6	1	5	16, 21, 22, 23*
Oil of theobroma, 50 per cent	6	3	3	5, 9, 9
Wool fat, 50 per cent	6	6	0	.....
Petroxolin, 50 per cent	6	2	4	6, 9, 13, 13
Vanishing cream, 25 per cent	6	1	5	7, 9, 12, 15, 28
U. S. P., 25 per cent	7	7	0	.....

* The fifth patient in this group had gingivitis throughout, but not definite salivation.

TABLE 4.—*Median Urinary Excretion and Range of the Cumulative Excretion for the Ninth Day for All Patients Given Inunctions with 50 Per Cent Ointments*

Group of Patients	Number of Patients	Median Excretion, Mg. of Mercury	Range, Mg. of Mercury
All	34	0.71	0.15 to 2.48
All white	22	0.93	0.15 to 2.46
All Negro	12	0.62	0.33 to 2.48
All male	26	0.71	0.22 to 2.48
All female	8	0.68	0.15 to 2.25
Male white	16	0.86	0.22 to 2.46
Female white	6	1.0	0.15 to 2.25
Male Negro	10	0.71	0.33 to 2.48
Female Negro	2	....	0.44 and 0.46

tion sufficiently. There was little or no relation to the relative level of excretion of mercury.

Influence of Race and Sex.—In our previous paper on inunctions [1] we attempted to study the influence of race, sex and cutaneous lesions on the absorption of the mercury, i. e., on the urinary excretion, so far as the data then available permitted. The close correspondence of the medians of the urinary excretion after inunctions of the various 50 per cent ointments allows us now to lump these together and thus secure a larger number of comparable data. In order to include the patients whose tests were discontinued relatively early because of salivation, the cumulative data on excretion during the first nine days were taken as the criterion (table 4).

It will be seen that the extremes for each group varied much more than the medians for the different groups. However, some of these differences appear significant.

The median for the white patients (0.93 mg. of mercury) was about 50 per cent higher than that for the Negro patients (0.62 mg. of mercury). The median for the white men (0.86 mg. of mercury) was also somewhat higher (21 per cent) than that for the Negro men (0.71 mg. of mercury). In the previous series of tests of inunctions the white group also appeared to have a definitely greater excretion in the urine than the Negroes. The difference, therefore, appears significant, indicating either that the white patients rubbed more vigorously or, what is more probable, that the white skin (especially with respect to the glands) facilitates the absorption of the mercury, as was suggested in our previous paper.[1] No difference was apparent as regards sex. The median for all the men (0.71 mg. of mercury) was practically the same as for the women (0.68 mg. of mercury).

TABLE 5.—*Correlation of Cutaneous Rashes with the Urinary Excretion of Mercury*

Type of Eruption	Level of Excretion	Median Index*
Follicular	++,+,+,N,†—	+0.6
Macular	+,N	+0.5
Squamous	++,—	+0.5
Papular	+++,+,+,N,N,N,N,—,—	+0.3
Papulosquamous	N	0
Maculopapular	N,—,—	—0.7
Sum of all except follicular rash	+++,++,+,+,+,N,N,N,N,N,N,N,—,—,—,—,—	+0.2

* The median index is the algebraic sum of the signs (N being considered as zero) divided by the number of patients showing the eruption.

† N indicates that the excretion was close to the median. The number of plus and minus signs indicates the divergence.

Effect of Cutaneous Eruptions on the Absorption of the Mercury.—Cutaneous eruptions were present in six of the patients who received inunctions with the 50 per cent ointments. In three of these the excretion was about the median level for the ninth day (0.71 mg. of mercury), namely, one with a squamous eruption (0.68 mg. of mercury), one with a papulosquamous eruption (0.46 mg. of mercury) and one with a maculopapular eruption (0.58 mg. of mercury). In the other three patients the excretion was notably high—from two to three times the normal amount. One of these had a maculopapular rash (1.67 mg. of mercury), and the other two had a follicular eruption (1.93 and 2.48 mg. of mercury, respectively). If these few cases are representative it would appear that follicular dermatitis distinctly increases the absorption of mercury from the inunctions, that the squamous rashes do not affect it, and that the maculopapular eruptions cause varying results. However, the number of cases would make conclusions very question-

able. We have, therefore, brought together the records of all our patients with a cutaneous eruption who were given mercury inunctions and compared the mercurial excretion with the medians for the patients having the same medication. The data in table 5 confirm the impression that the patients with follicular eruptions have the highest excretion—definitely higher than all others together or than those with a papular rash.

CONCLUSIONS

1. It may be concluded that the ointment bases, including fats of such widely different physical and chemical character as anhydrous wool fat, oil of theobroma, petroxolin and vanishing cream, have no significant effect on the absorption of the mercury. The choice between these may, therefore, be governed purely by the esthetic considerations and by the ease of inunction. The softer ointments require less labor, but care must be taken in their storage lest the mercury settle out.

2. Variations in the fecal excretion after inunctions are due chiefly to the accidental conveyance of the ointment to the mouth on the hands. This varies with the relative taste of the ointment and with the amount that adheres to the hands.

3. The incidence of salivation varies in the different series; this is not based on difference of absorption.

4. The absorption of the mercury is distinctly greater in the white patients than in Negroes (men), although the difference is not practically important. No differences appeared for the sexes.

5. Follicular cutaneous lesions apparently favor the absorption of inunctions; papular and other rashes probably have no effect.

INUNCTIONS WITH MERCURY OLEATE OINTMENTS

In a previous paper [3] we reported studies of excretion following the use of several mercury oleate ointments. These studies were undertaken primarily to test a suggestion which had been made by several authors, namely, that the absorption of mercury from the official ointments is due chiefly to the small quantity of oleate which they ordinarily contain. This was shown to be without foundation. Absorption of mercury occurred after inunction with oleate, but it was not materially better than that occurring with metallic mercury. The proportion of oleate in the official ointment being relatively small, it would play a correspondingly insignificant rôle in the therapeutic effect. However, the oleate appeared to offer therapeutic possibilities if the dosage were increased to effective levels. This might have practical advantages, since the application of the oleate would be less conspicuous and would not require prolonged friction. The mercury content of the official oleate (U. S. P.) amounts to 23.17 per cent, which is about equivalent to that of the mild

mercurial ointment. It is liquid and inconvenient for inunctions, and when it is made into an ointment it is, of course, further diluted. However, this may be offset by using a larger quantity and anointing a larger surface, an expedient which increases the efficiency, as we confirmed by studies of excretion following inunction with metallic mercury ointment.[2]

MATERIAL AND METHODS

Mr. E. D. Davy of the School of Pharmacy of the Western Reserve University prepared an ointment of good consistency containing 26.8 per cent of the oleate (6.2 per cent of mercury) in vanishing cream, so that 15 Gm. of the finished ointment corresponded to 4 Gm. of oleate, or practically 1 Gm. of metallic mercury. The formula is as follows: oleate of mercury in vanishing cream, 4 Gm. of oleate in 15 Gm. of ointment; potassium carbonate, 3.3 Gm.; sodium borate, 0.5 Gm.;

TABLE 6.—*Excretion of Mercury After Inunctions of 1 Gm. of Mercury (As Oleate Ointment) Daily*

Daily Level of Excretion (Median)		
Week of Treatment	Urinary Mercury, Mg.	Fecal Mercury Mg.
1	0.48 (0.07 to 0.92)	0.23 (0.06 to 0.56)
2	0.74 (0.24 to 1.76)	0.30 (0 to 0.46)
3	1.19 (0.53 to 2.55)	0.30 (0.12 to 0.92)
4	1.49 (0.54 to 3.22)	0.51 (0 to 0.90)
1 week after	1.55 (0.43 to 1.86)	0.26 (0.10 to 0.35)

Cumulative Urinary Excretion					
Patient	Days of Treatment	Mercury, Mg.	After-Period, Days	Mercury, Mg.	Total, Mg.
ARI	15*	15.42	6	6.41	21.83
WCSN	30	42.32	6	10.72	53.04
JRD	30	24.65	6	6.81	31.46
CHY	21	7.09	7	5.10	12.19
Cumulative Fecal Excretion					
ARI	15*	3.47	6	2.29	5.76
WCSN	30	10.94	6	2.50	13.44
JRD	30	6.82	6	8.92	15.74
CHY	21	6.25	7	3.34	9.59

* Salivation occurred on the fifteenth day.

stearic acid, 30 Gm. and water, 175 cc. When completed this yields 205 Gm. To the finished product, while hot, there is added 75 Gm. of oleate of mercury.

Series 1.—After a preliminary experiment with increasing doses to insure the safety of the procedure, the first series of observations was made on four male patients. Fifteen grams of ointment was rubbed daily into a larger surface of skin for thirty days or until salivation set in, and the urine and feces were collected daily. In one patient salivation occurred on the fifteenth day, and the inunctions were discontinued. Another was discharged after the twenty-first day without salivation. The other two received the inunction for thirty days without salivation. The detailed data for each patient were charted graphically but are not reproduced in order to economize on space. The most significant data are shown in table 6. These levels of excretion as well as the incidence of salivation showed that this is an effective therapeutic method.

It was next determined whether an ointment of half this strength would be effective.

Series 2.—A new ointment was made by the same general formula, but with half the amount of oleate, so that the 15 Gm. of ointment used daily contained

0.5 Gm. of mercury as oleate. This was used on seven patients. One had mild stomatitis on the ninth day, but this cleared up, although the inunctions were continued for thirty days. The most significant data are shown in table 7.

Series 3.—These values for excretion being considerably less than the anticipated half of those for the first series, a third series of tests was made, using

TABLE 7.—*Excretion of Mercury After Inunctions of 0.5 Gm. of Mercury (As Oleate Ointment) Daily*

Daily Level of Excretion (Median)

Week of Treatment	Urinary Mercury, Mg.	Fecal Mercury Mg.
1	0.04 (0.02 to 0.08)	0.03 (0.01 to 0.13)
2	0.07 (0.02 to 0.18)	0.06 (0.03 to 0.20)
3	0.07 (0.04 to 0.41)	0.09 (0.03 to 0.23)
4	0.11 (0.03 to 0.97)	0.13 (0.05 to 0.45)
1 week after	0.15 (0.02 to 0.59)	0.05 (0.02 to 0.25)

Cumulative Urinary Excretion

Patient	Days of Treatment	Mercury, Mg.	After-Period, Days	Mercury, Mg.	Total, Mg.
HRY	30	1.12	7	0.17	1.29
GEL	30	1.92	7	1.72	3.64
JHE	30	9.27	7	5.23	14.50
TCS	30	3.89	7	1.08	4.97
TTL	30	1.84	7	0.40	2.24
EHY	14	0.65	7	....	....
EPT	30	1.05	7	0.34	1.39

Cumulative Fecal Excretion

HRY	30	1.95	7	0.36	2.31
GEL	30	2.62	7	0.14	2.76
JHE	30	2.85	7	0.74	3.59
TCS	30	5.25	7	1.27	7.52
TTL	30	1.11	7	0.25	1.36
EHY	14	0.36	7	....	....
EPT	30	2.21	7	0.84	3.05

TABLE 8.—*Excretion of Mercury After Inunctions of 1 Gm. of Mercury (As Oleate Ointment) Every Other Day*

Daily Level of Excretion (Median)

Week of Treatment	Urinary Mercury, Mg.
1	0.03 (0.02 to 0.12)
2	0.18 (0.08 to 0.36)
3	0.29 (0.16 to 0.70)
4	0.47 (0.23 to 1.87)
Thirtieth day	0.52 (0.30 to 1.22)
One week after	0.52 (0.19 to 1.77)

Cumulative Urinary Excretion

Patient	Days of Treatment	Mercury, Mg.	Mercury in 7 Day After-Period, Mg.	Total Mercury, Mg.
MME	30	4.09	1.94	6.03
SSS	30	18.66	13.68	32.23
LGN	30	7.68	5.38	13.07
JFD	30	6.49	3.98	10.47
JMN	30	8.23	3.06	11.29
CPK	30	4.37	1.14	5.51

an ointment of the original concentration, containing 15 Gm. of oleate, or 1 Gm. of mercury, on alternate days. Six patients were treated for a period of thirty days, but only the urine was collected. In none of these patients did salivation occur. The significant data are shown in table 8. The results were intermediate between those of the other two series. We cannot give a conclusive explanation of these discrepancies, except that the official mercury oleate is not a chemical

entity, that it may contain different compounds according to uncontrollable variations in its manufacture and that these may vary in absorbability. It is also possible that the discrepancies are due to accidental variations in the patients, as the levels of excretion of the individual patients overlapped considerably in the differenct series, as will be seen from the tables.

COMPARISON OF THE DATA

The comparison of the medians obtained in these studies of oleate with those of former series and with those for ointments of metallic

TABLE 9.—*Comparison of Median Levels of Excretion of Mercury at End of the Fourth Week*

Inunction Method	Dose, Gm.	Percentage of Mercury in Ointment	Average Daily Dose of Mercury, Gm.	Urinary Excretion, Mg.		Fecal Excretion, Mg.	
				Daily	Cumulative*	Daily	Cumulative*
Oleate, 27 per cent	15, daily	6.7	1.0	1.49	14.6	0.51	8.9
Metal, massive	30, weekly	30	1.3	0.93	16.0	0.49	10.4
Metal, 50 per cent, U. S. P.	4, daily	50	2.0	0.83	10.7	0.45	13.5
Metal, 50 per cent, all vehicles	4, daily	50	2.0	0.84	11.5	0.41	8.3
Metal, 25 per cent, U. S. P.	4, daily	25	1.0	0.46	7.5	0.43	6.8
Oleate, 27 per cent	15, alternate days	6.7	0.5	0.47	7.1	....	...
Metal, 5 per cent	4, daily	5	0.2	0.146	2.1	0.25	5.3
Oleate, 20 per cent	4, daily	5	0.2	0.143	3.4	0.15	3.5
Oleate, 13.5 per cent	15, daily	3.35	0.5	0.11	1.7	0.13	2.4

* In this column is indicated the total amount of mercury excreted in this time.

TABLE 10.—*Median Levels of Excretion of Mercury at the End of the Fourth Week, Reduced to the Basis of Inunction of 1 Gm. of Mercury Per Day*

Inunction Method	Dose, Gm.	Percentage of Mercury in Ointment	Average Daily Dose of Mercury, Gm.	Urinary Excretion, Mg.		Fecal Excretion, Mg.	
				Daily	Cumulative*	Daily	Cumulative*
Oleate, 27 per cent	15, daily	6.7	1.0	1.49	14.6	0.57	8.9
Oleate, 27 per cent	15, alternate days	6.7	0.5	0.94	14.2	....	....
Oleate, 20 per cent	4, daily	5	0.2	0.72	17.0	0.75	17.5
Metal 5 per cent	4, daily	5	0.2	0.73	10.5	1.25	26.6
Metal, massive	30, weekly	30	1.3	0.70	12.0	0.37	7.8
Metal, 25 per cent, U. S. P.	4, daily	25	1.0	0.46	7.5	0.43	6.8
Metal, 50 per cent, U. S. P.	4, daily	50	2.0	0.42	5.4	0.23	6.8
Metal, 50 per cent, all vehicles	4, daily	50	2.0	0.42	5.8	0.22	4.2
Oleate, 13.5 per cent	15, daily	3.35	0.5	0.22	3.4	0.26	4.8

* In this column is indicated the total amount of mercury excreted in this time.

mercury illustrates the therapeutic and scientific relations. In tables 9 and 10 the data at the end of the four week course were used as being most significant. The inunctions are arranged in order of magnitude of excretion. Table 9 shows that the highest levels of excretion were reached by the daily inunction with 15 Gm. of 25 per cent oleate ointment, massive inunctions with a 30 per cent ointment of metallic mercury and daily inunctions with a 50 per cent ointment of metallic mercury. At about half of this level comes that caused by ointments of 25 per cent metallic mercury and 27 per cent oleate applied on alter-

nate days. The lowest were the levels caused by the inunctions with 5 per cent metallic mercury and 20 and 13.5 per cent oleate, in the doses used. In table 10 a comparison is made of the relative absorbability of the ointments by referring the excretion to a unit dosage. The highest rank now falls to the oleate ointment, 15 Gm. of a 25 per cent concentration applied daily and on alternate days; at about three fourths of this level is 20 per cent oleate ointment, 5 per cent metallic mercury ointment and massive inunctions of metallic mercury; at about half the level are the 25 and 50 per cent ointments of metallic mercury, and lowest is the aberrant 13.5 per cent oleate ointment. It will be seen that but for this last exception the absorbability of the oleates ranks high but averages scarcely more that one-third better than 50 per cent metallic mercury ointment.

RATE OF DECLINE AFTER INUNCTIONS ARE DISCONTINUED

The observations reported in our earlier paper seemed to indicate that after the inunctions were discontinued the excretion fell more

TABLE 11.—*Level of Excretion of Mercury a Week After Discontinuance of Inunctions, as Percentage of the Level on the Last Day of Inunction*

	Urine, Mg.	Feces, Mg.
Metallic Ointment		
50 per cent, 4 Gm. daily	51	75
5 per cent, 4 Gm. daily	61	68
Massive, weekly	84	62
Oleate Ointment		
27 per cent, 15 Gm. daily	104	51
13.5 per cent, 15 Gm. daily	136	33
20 per cent, 4 Gm. daily	46	75

rapidly following the use of the oleate than following the use of the metallic mercury. The present, more numerous data, show that this was accidental. In the later series the level of excretion following use of the oleate fell more slowly, perhaps because of the greater surface involved. Indeed, the urinary excretion averaged higher a week after discontinuance than on the day when inunctions were stopped, as shown in table 11.

THE URINE-FECES RATIO

This averaged exactly the same (urinary mercury = 1.13 times the fecal mercury) for the cumulative excretion of the mercury applied in the form of oleate and metallic mercury.

CLINICAL COMMENT

The mercury oleate ointment is colorless, and when prepared by the formula given it is somewhat stiff. It does not spread readily over the skin if kept on ice; in fact, it has to be rubbed in. Despite this lack of spread the patient is surprised to find that the medicament is

rapidly absorbed, so that after from eight to ten minutes at the most, 4 Gm. has entirely disappeared. The skin is no longer greasy, and nothing shows. We believe that the use of such a preparation when mercury is being exhibited is most satisfactory, as it requires no cleansing of the skin following the inunction. Moreover, there would be no telltale stain of the skin or clothing. Indeed, in an experimental series of six cases it was found that 16 Gm. of the ointment could be rubbed in more rapidly, in between twenty-five and thirty minutes, than 4 Gm. of the official ointment. Moreover, no residue showed on the skin after the inunction.

CONCLUSIONS

1. The absorption (as judged by the excretion) of mercury is somewhat better (perhaps a third) from ointment containing oleate of mercury than from ointment of metallic mercury in equal dosage.

2. Adequate doses may be secured by the daily inunction of 15 Gm. of an ointment containing 1 Gm. of mercury in the form of oleate. A formula for such an ointment with vanishing cream is described.

3. Inunctions with oleate require far less friction than do those with the metallic ointment and do not discolor the skin or clothing. We believe this to be a distinct therapeutic advance.

INUNCTIONS WITH COLLOIDAL MERCURY OINTMENTS

In an earlier paper [3] we reported contradictory data on excretion following inunctions with ointments of colloidal mercury and expressed the intention of checking these by further study. The results are herewith reported. A new specimen was used which may be called B in distinction to the earlier ointment, A; the two were prepared by a somewhat different technic by converting mercurous nitrate to oxide by the addition of sodium hydroxide, incorporating this oxide in hydrous wool fat and reducing with hydrazine hydrate. Analysis of this specimen B showed 45 per cent of mercury. A part was diluted with anhydrous wool fat to a 25 per cent ointment by Mr. E. D. Davy.

It may be recalled that the maximal size of the particles in the original ointment was reported as 8 microns, and the average size of the visible particles as 1.33 microns. We rather anticipated that this fine comminution would favor absorption, but we found that the urinary excretion with the undiluted ointment of 50 per cent colloidal mercury was about the same as that with the official 50 per cent ointment and that the absorption with the 25 per cent ointment of colloidal mercury was only one tenth of that of the 50 per cent ointment and about the same as that with the 50 per cent mild mercurous chloride ointment. This poor excretion holds for the new colloidal ointment B, there being but little difference in secretion between the 45 per cent and the 25 per cent strength.

It does not seem necessary to reproduce the detailed course of study of excretions which was made on six patients for each ointment during four weeks of inunction and a week following the tests, 4 Gm. of the ointment being applied daily for thirty minutes, under supervision, in the usual rotation of areas. The median level of excretion and the cumulative excretion at the end of the fourth week, as shown in table 12, arranged in order of magnitude of excretion, suffice for comparison. Since the urinary excretion with three of the four ointments was less than half that from the 5 per cent ointment of metallic mercury it is evident that they would be therapeutically useless; the better absorption of the one ointment would be only a disadvantage since it is unpredictable. This disadvantage is illustrated by the fact that in five of the six patients salivation occurred—in two, profusely. There was no salivation among those given inunctions with the B ointment.

That the colloidal mercury is not absorbed better than the globular mercury of the ordinary ointment may be explained by the relative

TABLE 12.—*Excretion of Mercury at the End of Four Weeks of Inunction with Colloidal Mercury Ointments and Comparison with Other Ointments* *

	Urine, Mg.		Feces, Mg.	
	Level	Cumulative	Level	Cumulative
50 per cent metallic mercury, U. S. P.....	0.83	10.7	0.45	13.5
50 per cent colloidal mercury, A.....	0.78	11.9	0.20	6.3
5 per cent metallic mercury, U. S. P., base..	0.15	2.1	0.25	5.3
25 per cent colloidal mercury, A.....	0.07	2.0	0.09	1.8
45 per cent colloidal mercury, B.....	0.05	1.3	0.13	2.5
25 per cent colloidal mercury, B.....	0.04	1.3	0.04	3.0
50 per cent mild mercurous chloride.....	0.05	1.3	0.11	10.7

* All the ointments were applied daily in equal quantities of 4 Gm.

rigidity of the colloidal particles, which may be less adapted to being squeezed and sucked into the hair follicles and ducts of the skin glands by the massage of the inunction. The difference between the results obtained with the A ointment of 50 per cent colloidal mercury, on the one hand, and those obtained with its dilution and the two B ointments, on the other hand, requires further explanation. It suggests chemical differences arising presumably through oxidation of the finely divided mercury in the manipulative procedures of the dilution of the A ointment and in the manufacture of the B ointment. Such changes are difficult to avoid and to a large extent are unavoidable when working with colloidal metals.

CONCLUSIONS

The absorption of mercury from inunctions with ointments containing 25 and 50 per cent of the metal in the colloidal state is variable but generally very poor, as indicated by the urinary excretion of only about a tenth of that excreted with the U. S. P. ointment. This would be therapeutically ineffective.

CONCLUDING REVIEW OF STUDIES OF MERCURIAL INUNCTIONS

These papers conclude the series of studies of mercurial inunctions. A brief general summary may, therefore, be desirable. It was the purpose in the investigations to compare the various methods of administration by varying the quantity and vehicle and by following the course of excretion of mercury as an index of the amount of actively circulating mercury. The urinary excretion gives the more reliable information, so the fecal excretion need not be further discussed although it was checked conscientiously throughout.

The comparison of treatments was complicated by the fact that the intensity of excretion varied greatly for different patients receiving the same medication, especially with inunctions, partly because of the difference in the skin and partly because of the variation in the vigor of friction. This was discounted by utilizing a sufficient number of patients to establish the type and by reducing the data to medians.

The studies of excretion confirm the clinical experience that inunctions with metallic mercury secure a smoothly ascending concentration of the drug, which declines rather slowly when the medication is discontinued.

The daily rotating inunction of 4 Gm. of the 50 per cent ointment for four weeks may be taken as the norm. The median daily excretion with this type of inunction was:

Mercury, Mg.	Week of Treatment
0.12	1
0.33	2
0.58	3
0.83	4
0.73	1 week after

The total urinary excretion in the four weeks is the most useful standard for the comparison of the different methods. The median for all the 50 per cent ointments amounted to 11.5 mg. of mercury; the nature of the vehicle did not alter this materially.

With the more dilute ointments the decrease in the excretion was fairly parallel with the mercury content.

Cleansing the skin with benzene after each inunction decreased the amount excreted by nearly half.

Massive inunctions, in which nearly the entire body surface was rubbed once a week with 30 Gm. of 30 per cent ointment, caused fully as high an excretion as the daily inunction with 4 Gm. of 50 per cent ointment, and the effective level was attained nearly a week earlier.

Colloidal mercury was absorbed unequally but never better than the metallic ointments and generally much less. It may be assumed that

the fluidity of the metallic mercury globules is important for pressing them in to the follicles.

The absorption of the colorless mercury oleate is of about the same magnitude as that of metallic mercury or about a third better. The oleate has the advantage of cleanliness, lack of detection and the far greater ease of inunction. We believe this to be a distinct advance if a mercurial ointment is to be employed.

The urinary excretion after the inunction of mild mercurous chloride ointment is so low that it could not be therapeutically effective.

Aside from the aforementioned findings on mercury oleate the end-result of these investigations confirms the clinical experience that the 50 per cent ointments of metallic mercury are the most effective form. The ointment vehicles are practically immaterial from the standpoint of efficiency, and they may, therefore, be chosen with reference to convenience. The fairly soft ointments are preferable as they are easier to apply, provided that they are sufficiently stiff to prevent the separation of mercury by gravitation. The removal of the excess of ointment with benzene diminishes the amount excreted, although apparently not below the effective level. The massive inunctions with 30 per cent ointment are fully as effective.

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EYELASH DYE

ILL EFFECTS AND SOME PROBLEMS EVOKED BY THEM

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The Journal of the American Medical Association [1] has within the past year published various clinical reports and made editorial comment on the ill effects of the use of certain eyelash and eyebrow dyes. For the most part, paraphenylenediamine or a related chemical has been thought to be the cause of these ill effects. It has seemed worth while to review the facts in the light of experimental work as well as to discuss some of the problems as they relate to the dermatologist.

Emile Berger [2] reported cases of disturbance of vision following the use of aniline hair dye. He noted that there were few cases reported of visual disturbance from aniline poisoning among aniline dyers and aniline factory workers. He reviewed the available literature and reported an instance of loss of visual acuity following dyeing of gray hair by a two-bottle aniline dye. He reviewed the reports of cases occurring in the aniline industry as well as those of persons using hair dye. He quoted Gautier, who in turn quoted Brocq who was given as the authority for the following case:

> A patient had a gray lock of hair dyed and, despite the fact that the dyed lock of hair was cut off, suffered from a general cutaneous reaction two and one-half months later. The last sentence of the paragraph is: "In mehren Fallen erfolgte der Tod"—"In numerous cases, death ensued."

No reference and no substantiation were given, but that thought is frequently expressed. Most compilers of the literature have failed to find cases with a fatal outcome following the use of hair dye of the aniline group. But one instance of death following the use of paraphenylenediamine for dyeing the eyebrows has been reported.

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1. Greenbaum, S. S.: Dermatoconjunctivitis Due to Lash-Lure, an Eyelash and Eyebrow Dye, J. A. M. A. **101**:363 (July 29) 1933. A Dangerous and Aniline Hair Dye, Report of the Bureau of Investigation, ibid. **101**:1016 (Sept. 27) 1933. Harner, C. E.: Dermato-Ophthalmitis Due to the Eyelash Dye Lash-Lure, ibid. **101**:1558 (Nov. 11) 1933. Jamieson, R. C.: Eyelash Dye (Lash-Lure) Dermatitis with Conjunctivitis, ibid. **101**:1560 (Nov. 11) 1933. What Price Eyes, Current Comment, ibid. **101**:1566 (Nov. 11) 1933. Certain Eyelash Dyes Prohibited, Medical News, ibid. **101**:1886 (Dec. 9) 1933. Sale of Poisonous Eyelash Dyes Prohibited, ibid. **101**:1975 (Dec. 16) 1933. Bourbon, O. P.: Severe Eye Symptoms Due to Dyeing the Eyelashes, ibid. **101**:1559 (Nov. 11) 1933. Moran, C. T.: Bilateral Necrosis of the Cornea Following the Use of Hair Dye on the Eyebrows and Lashes, ibid. **102**:286 (Jan. 27) 1934.

2. Berger, E.: Arch. f. Augenh. **50**:299, 1904.

Bab [3] asserted that the ophthalmologist is frequently consulted for acute and chronic disturbances of the eyes which can be traced to cosmetic procedures. Stop the cosmetics, and the irritation stops. All types of cosmetics—dyes, India ink, eyebrow pencils and henna dyes—are implicated. The reactions of six patients with severe conjunctivitis, edema of the eyelids and other severe disorders were traced to henna. Bab expressed the belief that the reaction can be explained by sensitiveness.

Dewey [4] reported an experimental study on the action of paraphenylenediamine hydrochloride, which is known to produce edema of the orbital tissue and bulging of the eyeball. The edema produced by paraphenylenediamine hydrochloride is essentially stasis of lymph, the result of which is dilatation of the lymph vessels. Birch-Hirschfeld was by this means able to demonstrate a lymphatic apparatus in the orbital tissue.

The symptoms arising from paraphenylenediamine poisoning bear a peculiar resemblance to those observed in poisoning from a group of substances collectively called histamines.

It would seem that paraphenylenediamine and histamine are too widely different for a common action. This action is common to a large group of poisonous substances of animal and vegetable origin. The fact that the edema from histamine poisoning is caused by histamine as a poison to capillary endothelium recalls that arsenic and gold salts are classed as capillary poisons.

The dog is the animal most susceptible to the toxic action of paraphenylenediamine introduced subcutaneously. The lethal dose is 0.1 Gm. per kilogram of body weight. One-half this dose is sufficient to produce marked symptoms. In the rabbit much larger doses are required, and the injection may be repeated, but ultimately the results are the same. Introduction of the drug directly into the circulation produces edema of the subcutaneous tissue, especially about the eye. The peculiar symptoms in the eye may also be produced by scarification of the skin, as, in fact, the effects of the hair dye on the skin would lead one to suppose.

The symptoms of paraphenylenediamine poisoning observed in dogs have been described by Grunert. The earliest and most striking symptoms are chemosis and exophthalmos with an increase of intra-ocular pressure. This is accompanied by increased lacrimal and mucous secretion of the conjunctivae and an increased flow of saliva. With a large dose the edema of the orbit passes over to the face and to the neck. There are

3. Bab: Deutsche med. Wchnschr. **59**:1041, 1933.

4. Dewey, K. W.: The Action of Paraphenylendiamin, Arch. Int. Med. **36**: 724 (Nov.) 1925.

vomiting, diarrhea, paralysis, trembling and apathy. With dyspnea and convulsions death occurs in coma within from three to six hours. Anatomically the poisoned animal shows serious effusions of the orbital cellular tissue, black discoloration of the lacrimal glands, slight brown discoloration of the tongue and gingivae, swelling of the entire mucosa of the upper air passages and, above all, edema of the tongue and the glottis. The other findings in the internal organs are in general irrelevant. Edema of the glottis is considered to be the cause of death.

There is no explanation as to the source of the edematous fluid. The edema fills the entire orbit as early as one hour after the injection and disappears again in one day without leaving a trace. It is stated that the orbital edema is congestion or stasis of normal lymph, which is apparently in a state of coagulation as it does not flow off when the edematous tissue is cut into.

Tainter and Hanzlik found that localization of the edema on the head and neck of the rabbit is not connected with an increased concentration of paraphenylenediamine in these regions since quantitative estimations of paraphenylenediamine in the saliva and in the edematous fluid showed the concentration to be less or no greater than in the blood plasma. They also stated that oxidation products are not concerned with the edema.

Dewey noted that the action of paraphenylenediamine seems to vary widely in animals. The strictly localized edema, the most conspicuous symptom in dogs, cats and rabbits, seems to have nothing in common with the nervous manifestations, the main symptom observed in guinea-pigs, frogs and mice, in which no edema occurs.

Dewey stated that the peculiar localization of the edema has received much attention but that no satisfactory explanation has been offered. The idea was advanced that the edema occurring in man and dogs is due to paralysis or irritation of the vasomotor nerves, resulting in an increase of vascular secretion. The edema in rabbits is marked about the face and neck. The localization may be due to differences in the constitution of the walls of the vessels in the involved area.

Dewey would have one compare the action of paraphenylenediamine with that of histamine. Intravenous injection of 10 mg. of the histamine hydrochloride in a cat produced immediate vomiting and purging, profuse salivation and labored respiration followed by a period of collapse. There is a marked idiosyncrasy in the species of animals, especially in the rodents. Observations on the reaction to histamine include the indications of a remarkable vascular action. Apparently histamine acts on two distinctly different anatomic structures in the vascular system. It causes a transient vasoconstriction in the arterioles and a more delayed and prolonged vasodilating action on the capillaries due to inhibition of their tone. The main action then consists in opening

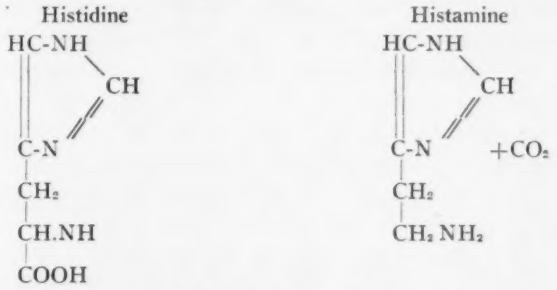
up new capillary areas together with permeation of the walls of the capillaries by blood plasma. The observation has been confirmed that there are a loss of plasma and an increase in concentration of red corpuscles in the blood as a result of the presence of histamine.

Paraphenylenediamine and histamine have another feature in common, namely, the striking dissimilarity in their action on different species of animals.

But one should not be misled. Abel and Kubota remarked: "The existence of these points of community, in the action of substances so utterly unrelated chemically as histamine and certain metallic ions, forbids any assumption that the production of similar effects by unknown constituents of some organ or tissue indicates the presence therein of histamine itself, or of any substance chemically related to it."

This caution is well worth remembering. As I review the effects of paraphenylenediamine and those of histamine I am reminded of my clinical and experimental findings in a case of thallium acetate poisoning. Of course, neither in paraphenylenediamine nor in histamine intoxication does one have the apparently specific action of a depilatory.

It seems warranted to review some of the little that has been published regarding histamine. Chemically it is beta-imidazolylethylamine. It is a base derived from the amino-acid histidine by the loss of carbon dioxide. Clark [5] said that the reaction which occurs is as follows:



Histamine is produced from histidine only when the latter substance loses its carboxyl group (COOH) before it loses its amino-group (NH_2). The effect is produced only by certain bacteria, and many bacteria possess the power of breaking down histamine. Consequently the amount of histamine produced when proteins are broken down by bacterial and other ferments is variable.

Traces of histamine can usually be found whenever there is a breakdown of protein. It is doubtful whether the quantity produced is sufficient to exert any pharmacologic action except in special cases. A moderate amount of histamine is found in ergot, and histamine is

5. Clark, A. J.: Applied Pharmacology, London, J. & A. Churchill, 1933, p. 610.

considered as one of the active principles of ergot, but the quantity is too small to have much action.

The effects of histamine and those of surgical shock, peptone poisoning and anaphylactic shock are similar. Some substances much like histamine and with a histamine-like action can be found in small traces whenever tissue is injured. Such a substance makes its appearance when tissues are injured by wounds or burns. It has been shown that this histamine-like substance is responsible for secondary shock after wounds. I would suggest in passing that the similarity of paraphenylenediamine poisoning and histamine poisoning may be due to the fact that intoxication with paraphenylenediamine produces the other.

In the meantime I note again that the sensitivity of different animals to histamine varies greatly, just as does their liability to suffer from anaphylactic shock and from paraphenylenediamine poisoning. The guinea-pig is readily killed by histamine; the mouse is tolerant of relatively enormous doses. There is unfortunately very little available information regarding the action of histamine on man. And, in fact, present available knowledge is insufficient to determine the relation between histamine and histamine-like substances which produce remarkably similar effects.

I wish to call attention to a condition of the skin about the eyes of a number of women which may have some bearing on this question of selectivity of ill effect of paraphenylenediamine. The condition is one of increased pigmentation and pruritus. The women all deny using eye cosmetic, hair dye or bleach but they do admit partaking of some coal tar derivative internally in the form of a sedative or antirheumatic. Acetylsalicylic acid has been a common home remedy, but I hesitate to inject it into the discussion because women of any group with any ailment—of the skin of the eyes or elsewhere—will admit taking acetylsalicylic acid.

Perhaps the coal tar derivative is insufficient by itself to cause the darkening of the skin about the eyes, but it may act as a catalyzer for sunlight or even for intense artificial light.

I have already reported my experience and clinical observations on perfume dermatitis. It required the combined action of a coal tar fraction in the perfume and sunlight to cause the pigmentation of the skin at the site of the application of the perfume and the exposure to the sun.[6]

This experience has been repeated several times: A physician who had frequently subjected himself to lengthy exposures to sources of intense ultraviolet rays with impunity had also taken neocinchophen with no ill effect on numerous occasions. One evening he took 15 grains

6. Goodman, H.: Perfume Dermatitis, Brit. J. Derm. **43**:177 (April) 1931.

(0.975 Gm.) of neocinchophen and exposed the skin of the entire body to the sources of ultraviolet. Within a few hours he had a generalized edema of the tissues and pain in the joints and was ill for six weeks, confined to bed.[7]

May there not be some concomitant insult which activates or permits the paraphenylenediamine to cause ill effects? This assumption might help answer the following question: Why do so few persons exposed to irritation by paraphenylenediamine show poisoning therewith? Certainly, 16 or 60 or 600 people who come under observation suffering with conjunctivitis and dermatitis from the application of paraphenylenediamine dye are but a handful compared with the thousands if not hundreds of thousands of women who have had dye applied to their eyelashes.

For six years or more I have more or less closely followed the medical aspects of cosmetics. During these six years no case has been called to my attention in which there was an untoward reaction due to an eyelash dye of the aniline group. Several years ago I sought for the cause of a dermatitis in an attendant of a cosmetic shop whose employer was the manufacturer of a two-bottle eyelash dye consisting of pyrogallol and an oxidizer. The manufacturer had been in business for more than twenty years, had used his application thousands of times and had done a large wholesale business to other cosmetic shops. No ill effect had ever been reported. No claim has even been made to the manufacturer's insurance broker for damage to the eye. The only claim ever made was that the dye was difficult to remove from the skin if it inadvertently reached the skin and that attempts at removal caused pain and distress.

As to the ill effect of paraphenylenediamine and other dyes of the same or similar composition, I have sought for two years to find an example in an active practice and in a clinic and have been unable to find one patient. I need some patients in order to make clinical application of some inhibition tests which I have worked out experimentally on animals.

I am acquainted with the ideas of allergy, but I doubt that they explain the appearance of dye dermatitis on the first contact with the dye. I am likewise acquainted with the term sensitivity; I prefer the old adage: "What is one man's meat is another's poison." I do not like to hide ignorance behind a well sounding phrase, but one seeks something on which to hang one's hat—some peg from which one can proceed. To return to a consideration of histamine for a moment: The decomposition of amino-acids can produce a series of basic products which have a strong pharmacologic action. Histamine is one of these bodies. It is the toxic base of histidine. The amino-acids are broken

7. Goodman, H.: Sun Tanning, Arch. Dermat. & Syph. **25**:15 (Jan.) 1932.

down by the liver. Perhaps a disease of the liver which may not be demonstrable by the comparatively crude tests of liver function causes the liver to be unable to detoxicate these substances. Such a theory implies a failure of an important cog in the physiologic machinery of health. It helps explain allergy and sensitivity. In the first instance the primary application of the dye or the drug causes a malfunction, which is allergy on a physicochemicophysiologic basis. In the second instance the malfunction is already present, which is sensitivity. In each instance a selective specific fault or a group fault is presupposed.

In the meantime some common detoxifying agent is needed or, better, an agent which will support, aid or assist the weakened detoxifying agent within the organism. One comes again to the two agencies—the insult and the soil. Whether it is paraphenylenediamine, histamine or thallium acetate, the ill effect depends on the soil which is reached. Given a proper detoxifying agency, there are no ill effects. Tremendous doses may overcome the best body defenses. One is left with the adage "One man's meat is another's poison," but one might add, "especially if it is too much meat or if the second person cannot digest meat."

FACTORS AFFECTING COLOR OF THE SKIN

THEIR SIGNIFICANCE IN BERLOCK DERMATITIS

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The mechanism of the development of berlock dermatitis has been the subject of repeated investigations since the first cases of this disorder were described by Freund. From these investigations has come the idea that oil of bergamot, which is one of the essential oils in eau de cologne and other perfumes, in some manner sensitizes the skin to the rays of the sun and thereby causes inflammation of the skin, which is usually followed by brownish pigmentation in the involved areas.

Freund and many investigators after him realized the therapeutic possibilities of the use of oil of bergamot, either alone or in alcoholic solution, combined with sunlight or ultraviolet irradiation, to produce pigmentation, in areas of the skin which had lost their normal content of pigment, as in vitiligo. Conflicting results have been reported.

In none of the investigations were the changes in color which took place recorded by any means except by visual observation. When an investigation is concerned chiefly with a comparison between slight variations in the degree of erythema and pigmentation, it is essential that a method more accurate than one of observation by the human eye be used to study and record the changes in color. Spectrophotometry affords such a method.

In the present investigation spectrophotometric analyses were made of the changes in color that took place in three areas of the skin which had been exposed to the same amount of irradiation from an air-cooled quartz mercury vapor arc lamp. One area was moistened with oil of bergamot before being exposed to ultraviolet radiation; the second area was moistened with a 10 per cent alcoholic solution of oil of bergamot before irradiation, and the third was treated only by irradiation

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* Now residing in Detroit.

The material in this paper was submitted by Dr. Rogin to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in dermatology. The work was done in the Division of Physics and Biophysical Research.

and thus served as a control for the two other areas. The area used as a control also gave information regarding the course of erythema and pigmentation in the normal skin after ultraviolet irradiation.

COLOR AND ITS ATTRIBUTES

The earlier methods of estimating color consisted chiefly in the use of color plaques; some methods were based on a definite system of color analysis, such as the Munsell disk or the Bradley top. Rowntree and Brown devised a skin tintometer consisting of nine separate color scales to which the tint of the area of skin under consideration could be compared. The matching was done under conditions least likely to introduce error, and the reading was then analyzed by the Munsell system of color measurement. Other color charts have also been used.

There are, however, certain objections to all these methods. The color vision of the observers enters as a factor, although to a less extent than in direct visual observation without the matching of colors against a standard. The methods depend on arbitrary pigmentary standards and not on pure spectral colors reflected from the skin. Such pigmentary standards in time always fade.

The analysis of color as made from the data obtained by spectrophotometry is a direct and accurate method for the quantification of color in terms of its fundamental attributes, namely, hue, brilliance and purity. Much information may be gathered from the plotting of curves showing the relationship between the spectral wavelength and the percentage of light reflected by the skin and by direct comparison of the curves thus obtained from corresponding areas of skin in different persons. However, if it is desired to describe accurately the color stimulus received by the observer in terms of the values for color excitation (red, green and violet), relative luminosity and purity, it is necessary to analyze the spectrophotometric reflection curve into its fundamental attributes of color. Such an analysis gives a scientifically correct description of the color. By suitable computations the spectrophotometric data may be converted so as to express these characteristics of color (Brunsting and Sheard *a* and *c;* Harris, Leddy and Sheard; Sheard, and Sheard and Brown).

The brilliance or relative luminosity (often spoken of as brightness, tint or value) defines the proportion of the total amount of standard white light which the material under test is capable of reflecting. In this manner the brilliance of the material under test may be classified as equivalent to some member of a series of grays, black and white being the extremes of the series.

The hue or dominant wavelength refers to that attribute of color which permits it to be classed as reddish, yellowish, greenish or bluish. The hue depends on the wavelength only.

The purity or saturation of a color defines the degree of hue which the color possesses. This attribute expresses the vividness or distinctness of a color and defines how red or how yellow, and so forth a color is. The Committee on Colorimetry of the Optical Society of America has discussed these and related subjects in complete detail, and further reference may be made to its report (Troland).

SPECTROPHOTOMETER

The details of the construction and operation of the spectrophotometer (Keuffel and Esser Color Analyzer) and of the principles underlying its use in the analysis of the color of the skin are to be found in the papers by one of us (Sheard) and his collaborators (Sheard, Sheard and Brown and Sheard and Brunsting). By adding a water-cooled cell Brunsting and Sheard (*a*) found it possible to examine spectrophotometrically living tissues without subjecting them to changes that might be induced by thermal radiation from the source of light (two 400 watt lamps) in the apparatus used.

CONVERSION OF SPECTROPHOTOMETRIC DATA INTO VALUES FOR COLOR EXCITATION

Probably the most fundamental data relative to color are those shown by the three color (red, green and violet) excitation curves reduced to an equal energy spectrum and referred to average sunlight at noon. Maxwell, Abney, and König and Dieterici were chiefly responsible for the fundamental developments regarding these relationships. Spectrophotometric data, read directly from the instrument as percentages of reflection, may be reduced to values for color excitation by the procedures given in detail in the report of the Committee on Colorimetry of the Optical Society of America (Troland).

SPECTROPHOTOMETRIC ANALYSIS OF COLOR OF THE SKIN

Sheard and Sheard and Brown found that in normal subjects the dominant wavelength, purity and percentages of the values for red, green and violet excitation, respectively, remained fairly constant. The value for relative luminosity varied according to the amount of pigment present in the skin. Subjects with much pigment in the skin reflect less light than those with little. Thus the values for relative luminosity of the skin of a Negro are low, whereas those for a blond person are higher. The values for the relative luminosity of the skins of brunette persons of the white race fall between those for the blond and those for the Negro. Variations in the amount of pigment do not affect the dominant wavelength (this is usually in the region of spectral yellow at 590 millimicrons) or the value for purity or saturation (approximately from

40 to 50 per cent). Brunsting and Sheard (*b*) obtained data from a series of determinations of the spectrophotometric reflection from the skins of persons of various races, including those of white persons, Negroes, Chinese and Indians. The authors found that the skins differed chiefly in the amount of pigment which they possessed. The amount of pigmentation may be taken as the reciprocal of the value for relative luminosity. The relative luminosities varied from 46 per cent in the blond to 7 per cent in the Negro. In all cases the values for dominant wavelength and purity of the color of the skin in the different races were approximately the same.

Brunsting and Sheard (*c*) also studied the part that superficial blood plays in the color of the skin. On the basis of a comparison of the reflection curves obtained from the skins of normal living subjects with those from postmortem specimens from which the blood had been removed, they attributed the zones of decreased reflection which they found in normal skin in the regions with wavelengths of 540 and 580 millimicrons to the presence of blood in the superficial capillaries, since these absorption bands correspond to those given by oxyhemoglobin. They also found that when there is an increase in the quantity of blood near the surface of the skin there is a decrease in the value for relative luminosity, just as there is when the amount of pigment is increased in the skin. However, in addition to the decrease in the value for relative luminosity, the increase in superficial blood causes other changes which an increase in the content of pigment does not produce. When there is an increase in oxygenated blood there is a shift of the dominant wavelength from the normal region of spectral yellow with a wavelength of 590 millimicrons toward the orange or red end of the spectrum with a wavelength of from 620 to 660 millimicrons. At the same time there is a decrease in the value for the purity or for the degree of the hue. If there is an increase of venous blood near the surface of the skin, as in cyanosis, the dominant wavelength shifts toward the blue region of the spectrum with a wavelength of from 490 to 500 millimicrons.

The results of Brunsting and Sheard and Sheard and Brunsting indicated that a decrease in the value for relative luminosity without an accompanying change in the two other fundamental attributes of the color of the skin signifies an increase in the pigmentary content of the area under investigation. The values for relative luminosity may be used, therefore, as a measure of the pigmentary content of the skin. The percentage of values for red excitation serves as an index of the degree of erythema present in the skin. The value for purity also may be used for this purpose, since the values for purity usually follow closely the course of those for red excitation. However, the use of the values for red excitation appears to be more logical when referring to the degree of erythema. Harris, Leddy and Sheard used these values

in this manner in their investigation of the erythemic and pigmentary changes of the skin after roentgen irradiation. We have followed the same procedure in this investigation.

LITERATURE CONCERNED WITH BERLOCK DERMATITIS

The literature concerned with berlock dermatitis is voluminous, and the reader therefore is referred to the bibliography. In general, the various writers are concerned with sensitizing substances, dermatitis venenata, individual susceptibility, sweat and fluorescent substances.

Berlock dermatitis has been ascribed to many causes. One of the most frequently cited explanations is concerned with the action of solar energy on sensitizing substances, such as eau de cologne and oil of bergamot, which may be present on the skin. Other investigators have concluded that the quantity and quality of solar radiation were not essential factors but that certain substances produced irritation of the skin similar to that in dermatitis venenata, which, when the dermatitis had subsided, left a residual pigmentation. This may occur in persons who possess hypersensitivity to certain irritating agents. The possibility of the irritating effects produced by combinations of bacteria and sweat or by sweat irradiated with solar energy has been suggested. Also, the presence of fluorescent dyes and oils in cologne water and in perfumes has been considered an etiologic factor.

PROCEDURE OF INVESTIGATION

The conflicting results of the attempts to produce berlock dermatitis and pigmentation in patches of vitiligo experimentally warranted the undertaking of the present investigation, since no previous reports had indicated the use of accurate quantitative methods of measuring the degrees of erythema and pigmentation, such as are possible with the spectrophotometer.

The skin of the volar aspect of both forearms was used because of the easy accessibility and the practical absence of hair on the volar aspect of the forearm in most persons. (When a great deal of hair is present, especially if it is dark in color, the value for relative luminosity is markedly reduced.) It was necessary to irradiate two areas on one arm and a third area on the other, since it was found that if all three areas were on the same arm one of them could not be placed flush against the aperture in the water-cooled cell of the spectrophotometer because of the hollow of the forearm at the wrist. The subject's arm rested on an adjustable support and was usually in the same position at each examination, that is, at about the level of the heart as the subject was seated at the instrument. A sandbag placed against the arm served to hold it in the correct position against the aperture.

The investigation was conducted during the summer, and therefore the subjects chosen were all men, since they could keep the forearms covered and thus protect the areas under examination from exposure to sunlight throughout the course of the investigations. All the subjects had latent syphilis but were free from cutaneous eruptions of any type. It was decided to use these patients as subjects since they had available the time necessary for the daily spectrophotometric examination,

as they were remaining at the clinic for antisyphilitic treatment. It was believed that neither the presence of syphilis nor the treatment instituted for this disease would alter the results of the experiment in any way. At the conclusion of the investigation for this group similar experiments were performed on thirteen normal and healthy young women and on eight normal and healthy men, whose skins represented many types from the very blond to the deep brunette. Exactly the same results were obtained in all these subjects as had been obtained in those of the syphilitic group.

Spectrophotometric readings of the skin in each of the three areas were made immediately before irradiation. Stencils of pliable tin were used to block off the areas to be irradiated and, at the same time, to protect the rest of the skin of the arm. The size of each area irradiated was 3.5 by 4 cm. This area was large enough to cover the aperture in the spectrophotometer. On one area natural oil of bergamot was applied before irradiation with the air-cooled quartz mercury vapor arc lamp. On the second area a 10 per cent alcoholic solution of oil of bergamot was applied before irradiation. These applications were made by gently wiping the area with a cotton-tipped applicator which had previously been moistened with the solution. Only a thin film of the liquid was applied to the skin, and it was allowed to remain for a minute or two before being exposed to ultraviolet radiation. The third area served as a control, and no solution was placed on it. All three areas were then exposed to exactly the same dosage of ultraviolet radiation from an air-cooled quartz mercury vapor arc lamp. The dosage employed had been found previously to produce moderate erythema in normal skin.

The next spectrophotometric reading ordinarily was made about six hours after irradiation. By this time erythema had usually appeared. Readings were then made twice daily for the next five or six days, once a day for the next week or ten days and every other day for the remainder of the tests, covering a period of from four to five weeks.

Applications of oil of bergamot and of the alcoholic solution of oil of bergamot were made on the upper part of the arm of each subject at some time during the experiment, but this application was not followed by ultraviolet irradiation. The areas were watched carefully for evidence of dermatitis.

Patch tests of the same liquids also were made on each subject, using squares of linen beneath gutta-percha and adhesive tape. These patches were allowed to remain on the upper part of the arm for twenty-four hours, and the area was then watched carefully from day to day for evidence of dermatitis.

EXPERIMENTAL DATA AND RESULTS

Experiment 1.—A man aged 63, with blue eyes, medium brown hair and fair skin on the unexposed parts, was exposed for two minutes to ultraviolet irradiation from the quartz mercury vapor lamp, operated at 125 volts and at a distance of 30 cm. Five hours later erythema appeared in all three areas, but it was definitely less marked in the area that had been moistened with oil of bergamot before irradiation. This difference in the degree of erythema was easily perceptible to the naked eye. However, it was impossible to discern any difference between the two remaining areas by visual observation alone. Spectrophotometric analysis showed that the greatest erythema, as measured by red excitation units (chart 1), appeared in the area used as a control to which no solution had been applied.

The peak of erythema was reached twenty-nine hours after irradiation in the area to which oil of bergamot had been applied. The curve showing the values for red excitation fell rapidly from this point. Schall and Alius found this sharp rise and sharp decline in 39.5 per cent of the cases in which they studied the course

of erythema produced by ultraviolet irradiation. They described it as a "crisis-like" reaction.

As the course of erythema was followed in this irradiated area from day to day, secondary maxima appeared, the peaks of which were reached on the fourth, eleventh and twenty-third days after irradiation. The curve for purity values followed closely, but in more accentuated form, that for the red excitation values. The curve for relative luminosity dropped sharply immediately after irradiation and reached its lowest point when the value for red excitation was at its peak. As the value for red excitation fell, the curve for relative luminosity rose. With several less marked secondary decreases in value it continued to rise until the thirteenth day, from which time it declined steadily until the nineteenth day. From

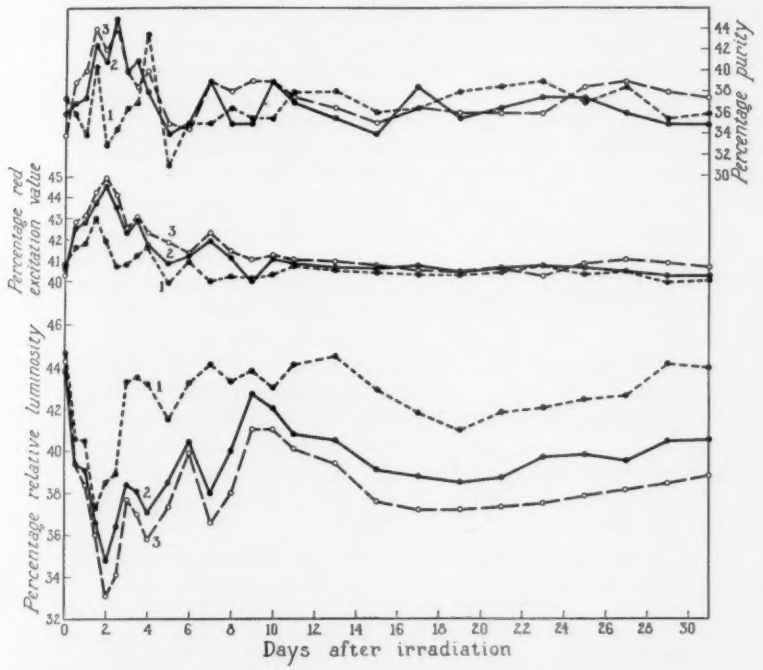

Chart 1 (experiment 1).—Curves showing values for purity, red excitation and relative luminosity. The same dosage of ultraviolet radiation from an air-cooled quartz mercury vapor arc lamp was used. Curves marked *1* represent values for the area moistened with oil of bergamot; curves marked *2*, those for the area moistened with a 10 per cent alcoholic solution of oil of bergamot, and curves marked *3*, those for the area directly irradiated.

this point the curve gradually rose until the conclusion of the investigation on the thirty-second day.

The value for red excitation for the area to which the alcoholic solution of oil of bergamot had been applied before irradiation showed an early increase which reached its maximal value forty-seven hours after irradiation. From this point it declined sharply, again in a crisis-like curve, but showed secondary increases, the peaks of which occurred seventy-seven hours after irradiation, and also on the seventh, tenth, seventeenth, and twenty-third days. As was found in the area first examined, the values for purity again followed closely those for red excitation.

The value for relative luminosity in this area dropped sharply from the onset and reached its lowest point at the time the value for red excitation was the highest, or forty-seven hours after irradiation. With several lesser secondary declines, the curve then gradually rose until the ninth day, after which it declined steadily until the nineteenth day; this point marked the beginning of a gradual rise in value which persisted until the end of the investigation.

In the area used as a control the increase in values for red excitation was greater than that which occurred in either of the two other areas. This curve was also crisis-like, with its highest point appearing forty-seven hours after irradiation and with secondary peaks on the seventh, tenth, twenty-first and twenty-seventh days after irradiation. As in the two areas already studied, the curve for the purity values again followed closely that showing the values for red excitation. Also, the curve for relative luminosity was rhythmic (wavelike) in character, with the low point reached forty-seven hours after irradiation (when the value for red excitation was the highest) and with other low points occurring four, seven and nineteen days after radiation. From the nineteenth day to the conclusion of the investigation on the thirty-second day, the value for relative luminosity increased steadily.

The values for green excitation units changed but little throughout the course of the entire investigation, whereas the values for violet excitation bore somewhat of a reciprocal relationship to those for the red; that is, when the values for red excitation were high the values for violet were low, and vice versa. The dominant wavelength varied between 582 and 593 millimicrons. In most instances the value of the dominant wavelength was found to be near 585 millimicrons, and the slight deviations from this value seemed to bear no relationship to changes in the values for the other attributes of color, that is, for purity or relative luminosity.

On comparison of the results obtained from the three areas examined in this subject, it is seen that the greatest erythema (value for red excitation) was found in the area used as a control, and that erythema in the area to which the alcoholic solution of oil of bergamot had been applied was only slightly less. The erythema in the area to which oil of bergamot had been applied was distinctly less than that in the other two cases.

The curves for relative luminosity, representing degrees of pigmentation, bear a reciprocal relationship to erythema or to the values for red excitation. The area used as a control reveals the lowest value for relative luminosity, whereas the value for the area to which oil of bergamot had been applied lies between those found for the other two areas.

The results obtained for the remaining subjects examined are similar to those obtained for this subject, which we have reported in some detail. It will be necessary to comment only briefly on a few variations which were encountered.

Experiment 2.—A man aged 48, with dark brown hair, brown eyes and a fair skin, was exposed for four minutes to ultraviolet irradiation from the quartz mercury vapor arc lamp, operated at 125 volts and at a distance of 30 cm. The curves for the values for red excitation rose rapidly and were sustained for approximately one hundred hours before falling. This curve is the plateau type, which Schall and Alius found in 12.5 per cent of their cases. There were only two secondary waves, and these also tended to be sustained. The curves for relative luminosity also showed division into definite maxima and minima.

Experiment 3.—A man aged 50, with dark brown hair, blue eyes and a medium complexion, was exposed for two minutes to ultraviolet irradiation from the quartz

mercury vapor arc lamp, operated at 125 volts and at a distance of 30 cm. The curve showing the values for red excitation in the area to which oil of bergamot had been applied was crisis-like and did not rise nearly as high as that in the other two areas. The curves for red excitation values in the other two areas showed an initial rise which reached its peak about twenty-four hours after irradiation and a second maximum, nearly as great as the first, about ninety-six hours after irradiation. Such curves fall into the group showing "double crisis" reactions, which Schall and Alius found in 20.5 per cent of their cases. In all three areas evidence of a rhythmic phenomenon was present in the curves for red excitation, purity and relative luminosity.

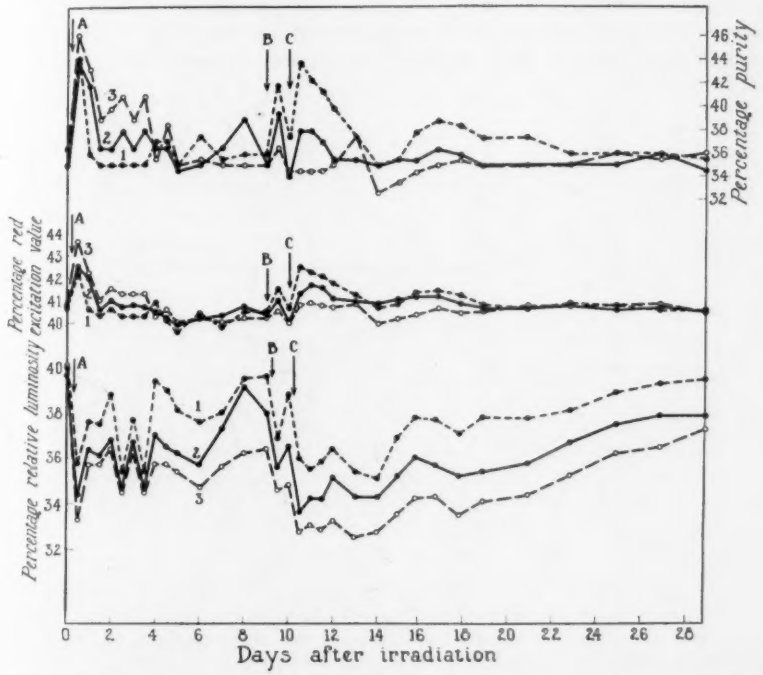

Chart 2 (experiment 4).—Curves showing the values for purity, red excitation and relative luminosity. At *A* ultraviolet irradiation (125 volts at a distance of 30 cm. for two minutes) was preceded by application of oil of bergamot in one area (curve *1*) and of a 10 per cent alcoholic solution of oil of bergamot in another area (curve *2*). An area directly irradiated was used as a control (curve *3*). At *B* ultraviolet irradiation only was used (125 volts at a distance of 30 cm. for four minutes). At *C* the same irradiation was used as in *B*, with ten minutes as the time of exposure.

For four other subjects studied in a similar manner the results obtained were the same as for the three subjects who have just been considered. Of the twelve areas studied in these four subjects, the curves for red excitation were crisis-like in nine, double crisis-like in two and plateau-like in one. Secondary waves were present in the curves showing the values for red excitation, purity and relative luminosity

obtained from all areas. In every case erythema and pigmentation were greatest in the area used as a control and least in the area to which oil of bergamot had been applied before ultraviolet irradiation.

Experiment 4.—A youth aged 17, with dark brown hair, brown eyes and a dark, swarthy complexion, was exposed to ultraviolet irradiation on three different occasions (chart 2). The initial exposure was preceded by an application of oil of bergamot in one area and of alcoholic solution of oil of bergamot in a second. The succeeding irradiations were given without applying solutions to any of the areas.

The initial reaction showed a sharp increase in the values for red excitation, which reached its maximal value six hours after irradiation and then dropped rapidly. This rapid fading of the erythema probably is explained by the protective action afforded by the patient's swarthy complexion. A second and larger dosage

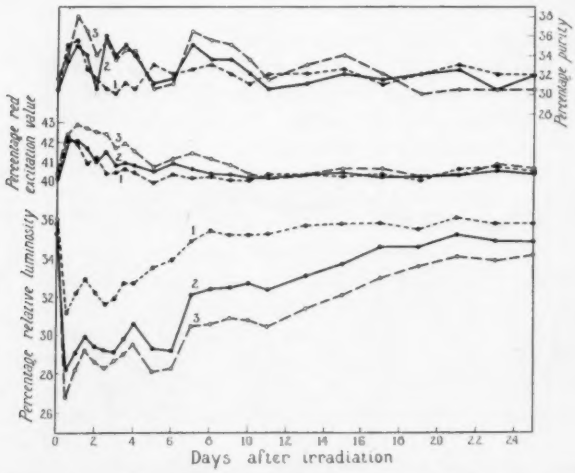

Chart 3 (experiment 5).—Curves showing the values for purity, red excitation and relative luminosity. Ultraviolet irradiation with 125 volts at a distance of 30 cm. was given for five minutes (curve *1*); for eight minutes (curve *2*), and for eleven minutes (curve *3*).

of ultraviolet radiation given on the ninth day produced the highest degree of erythema in the area to which oil of bergamot had been applied before the first ultraviolet irradiation. On the first occasion this area had shown the lowest degree of erythema and the least pigmentation. A third and still larger dosage of ultraviolet radiation given on the tenth day after the first irradiation again produced only a slight increase in erythema as measured by red excitation units. Apparently the pigment produced by the first ultraviolet irradiation acted as a protection against the subsequent exposures, since the larger doses gave much smaller erythematous reactions than did a much smaller dose applied to a nonirradiated (normal) area of skin. This observation is in agreement with the commonly accepted statement that normally dark-skinned persons or those with sun-tanned skins are not as susceptible to sunburn as are untanned or blond persons (chart 2).

Experiment 5.—A man aged 22, with blond hair, blue eyes and a fair skin which was well tanned from previous exposure to sunlight, was exposed to ultraviolet

irradiation from the quartz mercury vapor arc lamp. Solutions of oil of bergamot were not used on any of the areas, since the purpose of the test was to establish, if possible, a relationship between exposure to ultraviolet radiation and succeeding erythema and pigmentation. The curves for the red excitation values were crisis-like in all three areas. The highest value occurred in the area which had been exposed for the longest time, whereas the lowest value was that for the area which had been exposed for the shortest time. As in the other subjects, the values for relative luminosity were inversely proportional to the values for red excitation. Definite evidence of a rhythmic phenomenon was present in all three areas (chart 3).

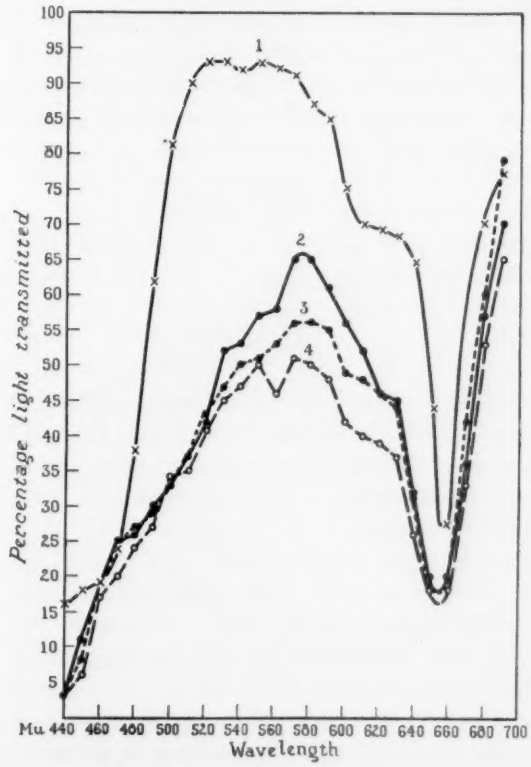

Chart 4.—Curves showing values for spectrophotometric transmission. Curve *1* represents the value for an alcoholic solution of chlorophyll from a green leaf; curve *2*, that for oil of bergamot before ultraviolet irradiation; curve *3*, that for oil of bergamot after ultraviolet irradiation (125 volts at a distance of 30 cm. for five minutes), and curve *4*, that for oil of bergamot after ultraviolet irradiation (125 volts at a distance of 30 cm. for one hour).

SPECTROPHOTOMETRIC CHANGES INDUCED IN OIL OF BERGAMOT BY ULTRAVIOLET IRRADIATION

Spectrophotometric analyses of oil of bergamot were made before and after ultraviolet irradiation to determine whether the irradiation caused any change in the solution (chart 4). The transmission of light

through the solution, as shown by curve 1, was markedly decreased in the spectral region with wavelengths of from 580 to 680 millimicrons, the lowest values of the absorption band being found in the region with wavelengths of from 650 to 660 millimicrons. This spectrophotometric curve is characteristic of the presence of chlorophyll in the solution under examination.

The effect of light on solutions of chlorophyll is shown by the changes in the spectrophotometric curve after ultraviolet irradiation. Decreased transmission, as determined by comparison of values with the data obtained before irradiation, was most marked in the spectral region with wavelengths of from 520 to 630 millimicrons. The characteristic absorption band at a region with a wavelength of 660 millimicrons remained unchanged. Spectrophotometric analysis of the irradiated oil of bergamot after it had stood overnight revealed no further change.

Spectrophotometric analyses were also made of the alcoholic solutions of oil of bergamot. These studies also revealed the presence of chlorophyll in the solution and indicated that the solution underwent a change after ultraviolet irradiation.

COMMENT

Effect of Application of Oil of Bergamot and a 10 Per Cent Alcoholic Solution of Oil of Bergamot to the Skin Before Ultraviolet Irradiation.—Analysis of the foregoing spectrophotometric data reveals that, irrespective of individual variations, certain features of the results are common to all the experiments.

The effect of application of oil of bergamot and that of an alcoholic solution of oil of bergamot to the skin before irradiation were similar in the eight cases in which this test was performed. Erythema and pigmentation were least marked in the area to which oil of bergamot had been applied. In the area to which an alcoholic solution of oil of bergamot had been applied, erythema and pigmentation were greater than in the area to which oil of bergamot had been applied, but they were less marked than in the area used as a control.

When these results are compared with those obtained in experiment 5, in which no solutions had been applied but in which graded doses of ultraviolet radiation were given, it is seen that the curves are markedly similar. It is evident, therefore, that the alcoholic solution of oil of bergamot lessens the results of ultraviolet irradiation by allowing less radiation to reach the skin beneath the solution. In effect this is the same as though a smaller dosage of ultraviolet radiation had been given in the first place. Oil of bergamot itself acts in the same manner as the alcoholic solution of the oil, but it decreases the effective value of the dosage still further. This confirms the observations of Felke,

Zurhelle (*a*) Sźantó and Gross and Robinson, for they noted the protective effect of solutions applied to the skin before irradiation.

The greater protective effect of the oil, as compared to that of the alcoholic solution, is undoubtedly explained on the basis of the greater concentration of the oil. The action of the solution in protecting the underlying skin against ultraviolet irradiation is probably purely that of an absorbing medium, since there are no changes in the curves for transmission other than a decrease in the percentage values, which is equivalent to a smaller dosage of ultraviolet radiation.

The differences in the reactions in each of the three areas were sometimes perceptible to the naked eye when the smaller dosages of ultraviolet radiation were given. When the larger dosages of ultraviolet radiation were given, enough of the rays penetrated the film of solution to cause marked erythema in all three areas. In such cases it was difficult by visual observation alone to detect which area showed the highest degree of reaction. The value of spectrophotometric studies was demonstrated in these cases. Differences in the reactions about seventy-two hours after irradiation in one of the subjects could be detected easily with the eye alone, and the degree of difference could be accurately recorded by means of the spectrophotometer.

A sensitizing action of oil of bergamot, or of its alcoholic solution, to ultraviolet radiation could not be demonstrated in any of the subjects studied, if the evidence of such action is based on a consideration of the increase of erythema and pigmentation in the area beneath the solution as compared to that in the area used as a control.

None of the subjects showed evidence of dermatitis after direct application of the solutions without ultraviolet irradiation or after patch tests performed as described earlier in the paper. It would have been of interest and of possible value to have studied spectrophotometrically a patient who had berlock dermatitis, but such a clinical case was not available.

Presence of Chlorophyll in Solutions of Oil of Bergamot.—The presence of chlorophyll in the solutions of oil of bergamot at once raises the question as to whether chlorophyll, which is commonly recognized as being sensitive to light, may also act as a sensitizer to the rays of light in cases in which changes in color of the skin occur during irradiation and during the period of time that the solution is on the skin. Proft found that erythema and pigmentation in the skin to which chlorophyll had been applied before irradiation were slightly increased over the reactions produced in the area used as a control. This increase was slight and of about the same degree as that in another area to which only pure water had been applied before irradiation. Proft expressed the belief that the sensitizing action of certain soft soaps containing chlorophyll could not be explained on this basis and that the mechanism for such

action must be sought in another direction. The sensitizing action produced by ingestion of chlorophyll (buckwheat) was demonstrated by Sheard, Caylor and Schlotthauer and by others, but more work is necessary before a similar action can be proved for the cutaneous application of solutions of chlorophyll followed by ultraviolet irradiation.

Rhythmic Phenomena in the Course of Erythema and Pigmentation.—Further analyses of the spectrophotometric data show that the initial erythematous reaction may be classified, according to the standards of Schall and Alius, as crisis-like in nineteen of the areas studied, plateau-like in four and double crisis-like in four.

Schall and Alius and Schall found marked individual variations in the course of erythema after ultraviolet irradiation. However, they noted definite evidence of a wavelike phenomenon, similar to that described by Miescher and others after roentgen irradiation, in 62 per cent of the fifty-five cases studied. They found a suggestive wavelike reaction in an additional 14 per cent of their cases, while in only 24 per cent was the phenomenon absent. The number of waves in each case was variable, but according to a chart included in their paper, from two to three definite waves occurred within the first one hundred and thirty-four hours after irradiation.

Schwarz expressed the belief that a secondary period of latency was not limited to erythema following roentgen or ultraviolet irradiation. He found a wavelike phenomenon in the course of the erythema of dermatitis induced by mustard oil. He stated that it is probably also present in other biologic reactions, such as in the reaction to tuberculin. According to his results the waves showing spectrophotometric phenomena in mustard oil dermatitis occurred over a period of hours rather than of weeks, as is the case after roentgen irradiation. He advanced no evidence for a wavelike phenomenon after ultraviolet irradiation.

Pohle studied the skin by means of the capillary microscope after a single exposure to a medium erythema dose of ultraviolet radiation. He made observations in two, six, twenty-four and forty-eight hours and in two weeks after irradiation. At the end of two weeks' time there was no pigmentation, and the capillaries had returned to the normal condition. He concluded from his investigations that the effect of uitraviolet irradiation on the capillaries was brief and temporary, and that there was but one cycle.

Evidence of a wavelike phenomenon in the course of erythema and pigmentation was present in each of the twenty-seven areas studied in this investigation. The individual variations in the time of occurrence of the waves were so great that no attempt was made to classify the waves according to the interval of time at which they occurred. In this respect the reaction after ultraviolet irradiation is apparently somewhat different from the effect of roentgen irradiation, in which the reaction

may be divided into at least three waves occurring at more or less definite intervals of time. The same dosage of ultraviolet radiation was given on only three occasions during the present investigation, and conclusions regarding definite intervals of time for the appearance of the waves can scarcely be drawn from such a small series. There is need for further investigation in this direction, a constant dosage of ultraviolet radiation in a large series of cases being used.

The amount of pigmentation which occurred in an irradiated area was directly proportional to the degree of erythema in that area. This was true only when different areas in the same subject were compared (experiment 5). Such a statement cannot be made when the degrees of erythema and pigmentation of different subjects are compared. A high degree of erythema may result in deep pigmentation in one subject, whereas approximately the same degree of erythema may produce only slight pigmentation in another subject. These observations on the marked individual variations in erythema and pigmentation after ultraviolet irradiation have been repeatedly noted in the literature and have been confirmed spectrophotometrically in the present investigation.

In general the course of the values for relative luminosity was also wavelike in character, but the waves were usually independent of those for red excitation. However, there was an initial sharp decrease in the value for relative luminosity which reached its minimal point at approximately the same time that the value for red excitation was at its maximum. Then, as erythema faded the value for relative luminosity increased. Brunsting and Sheard indicated that an increase in the quantity of blood in the peripheral vessels reduced the value for relative luminosity. This probably is the explanation for the initial sharp decrease in the value for relative luminosity. Since there was practically no change in the dominant wavelength (hue) in any of the areas studied, erythema must be chiefly, if not entirely, due to an increase in the quantity of blood in the peripheral vessels. The quality of the blood remains unchanged with respect to its content of oxygen. This statement is made on the basis of observations by Brunsting and Sheard that a reduction in the oxygen content of the blood, as in congestion (the presence of an increased amount of venous blood), causes a shift in hue toward the blue end of the spectrum, whereas an increase in the oxygen content of the blood, as in hyperemia (the presence of an increased amount of arterial blood), causes a shift in hue toward the red end of the spectrum. Since no change in the hue of the irradiated areas occurred at any time during the investigation, it must be concluded that the increased redness which follows irradiation is due to an increased amount of normal blood in the periphery. This is accomplished by an increase in the number of open capillaries and also by a more complete dilatation of capillaries already open. Harris, Leddy and Sheard advanced this

explanation for erythema that follows roentgen irradiation. Such a conclusion is further supported by the work of investigators who have studied the capillaries of the skin.

After the value for relative luminosity recovered from its initial sharp decrease, the curve continued independently of that for the red excitation value. Its course varied markedly in different subjects but showed a definite rhythm in all of them, indicating a peculiar lability in the pigmentary function of the skin. The variations from time to time may be explained in part by the difference in the amount of scaling which occurs normally at all times, the pigment being carried off in the scales. Such changes are particularly marked during hot weather, when increased perspiration carries with it an increased amount of the superficial layers of the skin.

CONCLUSIONS

1. The use of the spectrophotometer affords an accurate method of recording the changes of color in the skin after ultraviolet irradiation.

2. The initial erythematous reaction of the skin after ultraviolet irradiation is generally crisis-like in form, but may also be plateau-like or double crisis-like.

3. The course of the erythema is rhythmic or wavelike in nature and persists over a period of weeks.

4. In the same subject the amount of pigment formed after ultraviolet irradiation is proportional to the degree of the preceding erythema. This statement cannot be made, in the light of the data at hand, when erythema and pigmentation are compared in different patients after ultraviolet irradiation.

5. The changes in pigment follow a rhythmic course, apparently independent of the course of erythema.

6. There are marked individual variations in the chronology of the waves which appear during the course of erythema and pigmentation.

7. The hue of the skin after ultraviolet irradiation remains constant.

8. The changes in the redness of the skin after ultraviolet irradiation are due to changes in purity (saturation) of the hue.

9. The presence of chlorophyll in solutions of oil of bergamot was shown by obtaining curves for spectrophotometric transmission which are characteristic of chlorophyll. There was a decrease in the spectrophotometric transmission of solutions of oil of bergamot after ultraviolet irradiation.

10. Oil of bergamot and a 10 per cent alcoholic solution of oil of bergamot applied to the skin before ultraviolet irradiation diminish the effects of such irradiation.

11. Ultraviolet irradiation following applications of oil of bergamot and a 10 per cent alcoholic solution of oil of bergamot to the skin did not produce dermatitis or increased pigmentation in any of the cases studied.

12. It is suggested that berlock dermatitis belongs to the group of cutaneous reactions of the venenata type and that it is due to an individual hypersensitivity to chlorophyll or adulterants found in the perfume or toilet water which has been applied to the skin.

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MODIFIED COMPOSITION OF IODOBISMITOL

RESULTS ON LOCAL IRRITATION

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WITH THE ASSISTANCE OF P. S. POUPPIRT, M.D., AND M. R. SOMERS, M.D.

SAN FRANCISCO

Experiences in the use of iodobismitol (N. N. R.) during the past three years indicated the desirability of making a small change in composition in order to facilitate administration of the product, especially to sensitive patients. Most patients experience an initial sensation of burning at the site of injection, but a certain proportion of patients complain of sustained pain and apparently cannot tolerate the product. The following composition is proposed as the most satisfactory of a number tried: sodium iodobismuthite, 6 per cent, saligenin, 4 per cent, and sodium iodide, 12 per cent, dissolved in propylene glycol. Saligenin is a local anesthetic and practically nonirritant and nontoxic.[1] Propylene glycol is substituted for ethylene glycol in order to eliminate the potentialities of systemic toxicity from ethylene glycol. The modified preparation of iodobismitol, which is designated "iodobismitol with saligenin," has a greater viscosity than ordinary iodobismitol owing to the propylene glycol, but this is believed not to be objectionable.

A condensed summary is given in the table of results obtained with the various modifications of iodobismitol tried. Patients from clinics for the treatment of syphilis in the acute and late stage were used. Injections were given to 1,174 persons, of whom about 60 per cent were men, and the total number of injections was about 3,275. All injections were intragluteal, each of 2 cc. The schedule of injections was as follows: single injections of modified iodobismitol without comparison with iodobismitol; alternate injections in opposite buttocks of

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From the Department of Pharmacology and the Division of Neuropsychiatry, Stanford University School of Medicine.

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modified and original preparations of iodobismitol, and multiple successive injections of modified iodobismitol. Each group of patients was given the injections by the same person, but different persons gave the injections for different groups. Records were made of complaints by

Summary of Observations on Local Irritation in 1,174 Persons from Injections of Iodobismitol and Modified Compositions

Product Used	Number of Patients	Number of Injections	No or Fleeting Reaction,* Per Cent	Definite or Persistent Reaction,† Per Cent	Volunteer Comparisons with Iodobismitol		
					Same, Per Cent	Better, Per Cent	Worse, Per Cent
Iodobismitol‡.....	231	657	68.0	32.0			
Iodobismitol with 2 per cent benzyl alcohol...	215	512§	71.7	28.0			
Iodobismitol‡.....	200	545	68.8	31.0			
Iodobismitol with 2 per cent benzyl alcohol...	200	480‖	72.1	28.0			
Iodobismitol‡.....	106¶	...	63.8	36.2			
Iodobismitol with 2 per cent benzyl alcohol...	82¶	...	45.0	55.0	55.0	0.0	45.0
Iodobismitol with 4 per cent phenylethyl alcohol.....	15	...	80.0	20.0	53.4	33.3	13.3
Iodobismitol with 2 per cent saligenin.....	259	259	61.5	38.5	56.0	23.8	20.2
Iodobismitol with 2 per cent saligenin#.....	12	37	....	....	75.0	25.0	0.0
Iodobismitol with 4 per cent saligenin.....	120	143	67.5	32.5	55.9	35.8	8.3
Iodobismitol with 6 per cent saligenin**.....	105	105	74.0	26.0	53.0	35.0	12.0
Iodobismitol‡ with 33.3 per cent water.....	183	...	....	....	70.0	8.0	22.0
Iodobismitol‡ with 20 per cent water.....	166	...	....	....	60.0	20.0	20.0

* No objection was volunteered or there was not more than a fleeting sensation of local burning for from five to ten minutes.

† Complaints of burning, severe initial pain, stiffness of the legs, cramps in the legs, limping or persistent soreness and discomfort in the gluteal region persisted for from ten minutes to three days after the injection.

‡ Composition: sodium iodobismuthite, 6 per cent, and sodium iodide, 12 per cent, in ethylene glycol (iodobismitol). The other mixtures containing local anesthetics had the same salts in propylene glycol.

§ The patients in this group were the same as those of the preceding group who received iodobismitol.

‖ At least one injection each of iodobismitol and of the modified product was given to each patient in this group.

¶ Each patient in this group received from 2 to 4 injections.

This was a special group of private patients.

** Twenty-one patients of this group received 3 cc. doses.

the patients immediately after injection and after ten minutes, one hour, one day, two days and three days. Patients were asked to volunteer comparisons of the effect with that of the original preparation of iodobismitol, which they had received previously, but were not told the identity of the mixtures injected. In short, every attempt was made to obtain reliable evidence of the subjective reactions without bias or extraneous influences. The value of the data is limited by the uncer-

tainties of subjective sensations, individual variabilities (even in the same patient from time to time) and incomplete controls with the original preparation of iodobismitol in certain groups of patients. Considerable value may nevertheless be attached to the data because of the large amount of routine experience in these clinics with the original preparation of iodobismitol. Nearly all groups of patients were given injections by experienced persons who had given injections of iodobismitol to thousands of patients under many conditions. The majority of patients were men. Probably about 10 per cent more women than men complained of pain under all conditions of the tests, and if the groups had been larger this small difference might have been eliminated. Therefore, the observations on the women and on the men have been grouped together, which gives the summary greater statistical value.

The summary in the table indicates the relative advantages offered by iodobismitol prepared with propylene glycol and containing 4 per cent saligenin. Nearly all other modifications tried—namely, the addition of benzyl alcohol, 2 per cent, saligenin, 2 per cent, and two dilutions with water—made little or no difference from the effect of the original preparation of iodobismitol. Phenylethyl alcohol, 4 per cent, gave about the same results as saligenin, 4 per cent, but the number of cases was far too small to warrant any conclusions. The benzyl and phenylethyl alcohols are rather irritating, and this irritation could not be reduced by using higher concentrations. Both of these alcohols are rather unpleasant in the reaction on the tongue, causing marked biting and burning, which is not true of saligenin. The aqueous dilutions of iodobismitol reduced the hypertonicity of the original product but did not improve on the irritation of the latter. Saligenin itself was found to be practically nonirritating. Its local anesthetic action was quite pronounced, as claimed by Hirschfelder and his associates,[1] who found its effect to be comparable with that of procaine hydrochloride. A local anesthetic action is quite pronounced on the tongue and gums. A higher strength, namely, 6 per cent, had no advantage over the 4 per cent strength, which was finally adopted. Several assisting physicians volunteered the opinion that iodobismitol with saligenin was the only modification which made a difference in the complaints of irritation.

It is possible that a systemic action from the saligenin resulting in from mild to moderate analgesia assists the local anesthetic action. While a dose of 80 mg., which is given with each injection of iodobismitol, is comparatively small for an average adult, an analgesic action might be exerted in a sensitive person. On the other hand, such analgesic action is lacking with benzyl and phenylethyl alcohols, which are readily conjugated, i. e., detoxicated, in the body even when used in fairly large doses. Thus, there are good grounds for believing in the superiority of saligenin for the purpose.

Procaine hydrochloride and related local anesthetics cannot be used in a mixture with iodobismitol since precipitates are formed and since they are also more toxic than saligenin. Therefore, saligenin possesses definite advantages which may be utilized to mitigate the irritation of iodobismitol. It is believed that iodobismitol with saligenin should be given a period of trial by physicians generally, since a wider experience would be useful in determining the ultimate choice of an acceptable modification of iodobismitol. Iodobismitol with saligenin may be used in place of ordinary iodobismitol in the treatment of syphilis.

SUMMARY

The following modified form of iodobismitol is offered for use in the treatment of syphilis in the same way as iodobismitol (N. N. R.): iodobismitol with saligenin, containing sodium iodobismuthite, 6 per cent, sodium iodide, 12 per cent, and saligenin, 4 per cent, in propylene glycol. The saligenin acts as a relatively nontoxic and nonirritant, though efficient, local anesthetic, and the propylene glycol eliminates all potentialities of systemic or cumulative toxicity sometimes attributed to ethylene glycol.

Comparative observations on 1,174 clinical patients indicated a better tolerance of iodobismitol with saligenin than of iodobismitol (N. N. R.) and of a number of other modifications tried.

Clinical Notes

URTICARIA, EDEMA AND PURPURA FOLLOWING SMALL DOSES OF DI-NITROPHENOL

Report of a Case

MAURICE HENRY NOUN, M.D., DES MOINES

There have been numerous cases reported during the past few months of intoxication produced by di-nitrophenol. This has manifested itself in the form of jaundice, agranulocytic angina, urticaria or maculopapular eruptions following the ingestion of the drug. In several instances death has occurred.

No mention has been made, however, of any cases in which purpuric lesions developed along with the urticarial eruption. I therefore wish to submit a report of a case of eruption following the ingestion of di-nitrophenol.

REPORT OF CASE

Mr. H. G. A., aged 40, a patient of Dr. Laurence Smith, normally weighed 175 pounds (79.4 Kg.) but had gained in weight so that when seen by Dr. Smith his weight was 240 pounds (108.8) Kg.).

On April 27, 1934, the patient was given 2 grains (0.13 Gm.) of di-nitrophenol daily with a dietary restriction. His general physical condition was good. There was no history of allergy. The basal metabolism on April 30 was plus 10. The urine and the blood chemistry were normal. The patient was told to report any untoward symptoms such as excessive perspiration or feeling of weakness or dizziness. The basal metabolic rate on May 3 was plus 23.

On May 19 he first noticed marked generalized urticaria and complained of severe itching. His face was edematous, and his eyelids were closed. His hands and feet were edematous to such an extent that he was unable to put on his shoes. On the dorsum of the feet extending toward the ankles and on the lower third of the legs were numerous, scattered petechiae the size of a pinhead. These purpuric spots were not present anywhere else. A blood count made at this time was found to be normal except for a slight decrease in the number of blood platelets.

The patient was given 0.5 cc. of epinephrine, and shortly after that many of the urticarial lesions disappeared. Some of the edema about the face and ankles also subsided. He was advised to take frequent colloidal baths of oatmeal gruel and bicarbonate of soda. This was followed by a local application of a soothing lotion. He was given a moderate dose of magnesium sulphate twice that day.

The following morning he was well enough to appear at the office. Hemorrhagic spots the size of a pinpoint were still present about the ankles and legs. The swelling and urticarial lesions had subsided to a considerable extent. The patient refused to cooperate by having cutaneous tests or giving blood for an experiment in passive transfer.

COMMENT

The patient received 2 grains of the drug per day, which is half the dose prescribed as a safe one, yet symptoms developed in a short time. The dose of the drug is therefore no absolute guide for harmful effects. In this case

there may have been cumulative effects or biotropic effects of the type described by Milian. The most probable explanation is, however, that the patient became sensitized to the drug. Frumess [1] has recently been able to demonstrate Prausnitz-Küstner antibodies in a case in which small doses of the drug caused an eruption.

Robinowitch [2] in a recent editorial brought out the fact that it is difficult to predict the toxicity of this drug. He stated that the same amount not only may affect persons of the same body weight differently but may act differently in the same person on different days.

CONCLUSION

Alpha-di-nitrophenol is a dangerous drug and should not be used promiscuously. Symptoms pointing to sensitization may develop rapidly. Purpura with marked urticarial lesions developed in my patient. Untoward symptoms may appear even though the patient is carefully observed.

1. Frumess, G. M.: Allergic Reaction to Dinitrophenol, J. A. M. A. **102**:1219 (April 14) 1934.

2. Robinowitch, I. M.: The Dangers from Dinitrophenol, Canad. M. A. J. **30**:564 (May) 1934.

DERMATITIS DUE TO HYACINTH BULBS

DAVID W. JOHNSON, M.D., WHITE PLAINS, N. Y.

Mr. B., aged 34, complained of an eruption which for about six weeks had involved the distal ends of the fingers. Examination revealed dry, scaly lesions with deep fissures, especially beneath the finger-nails. The lesions were at no time vesicular, but they became erythematous and dry. There were no other lesions on the body. The patient also complained of intense itching of both ears.

The patient was employed as a clerk in a bulb and seed store and frequently handled bulbs. On September 15, after receiving a supply of hyacinth bulbs, he noticed the eruption.

Samples of the bulbs were obtained and macerated. Patch tests were made in the usual manner, with the pulp and with the outer leaf. The macerated pulp, especially that of the Dutch hyacinth, produced a definite erythematous and slightly raised eruption at the site of contact. It is interesting to note that the patient complained of intense itching of the ears and of the site of contact about five minutes after the application of the patch.

Minor Notes

FORMULA FOR GLYCEROGELATIN DRESSING

WILLIAM ALLEN PUSEY, M.D., CHICAGO

In response to the note on zinc glycerogelatin dressings in the May issue of the ARCHIVES (**31**:701, 1935) a well known dermatologist makes the point that "there are almost as many formulas as there are textbooks," and asks me to "let the readers of the ARCHIVES in on the secret of your preference."

For many years I have used the following formula with satisfaction:

	Parts
Mixed zinc oxide and calamine (for its color)	15
Gelatin	28
Glycerin	28
Water	29

Approximately 2 ounces of zinc oxide, 2 ounces of calamine, 8 ounces of gelatin, 8 ounces of glycerin and 8 ounces of water are required to make a 24 ounce batch. To this is added 30 drops of phenol as a preservative; the phenol has never proved irritating. The mixture is put in a water bath at boiling temperature and slowly dissolved with stirring. Water is added to compensate for evaporation. After the mixture is well dissolved, it is strained though gauze to get rid of all rough particles, and then, as an extra precaution, it is sterilized under pressure in an autoclave. This preparation will keep indefinitely and stand innumerable reheatings. The secret of satisfactory experience with the dressings lies in having it of a proper consistency; when melted, it should be thin enough to apply to the skin without dragging of the brush. This consistency can be maintained by adding water, as the circumstance may require, to the melted dressing.

The application of the dressing can be finished without waiting for it to harden. Paint on the gelatin in a thin coat and immediately cover with absorbent cotton until no sticky points are exposed, leaving only a moderate excess of cotton on the surface; powder freely with talcum powder and then put a stocking or bandage over the whole surface. The application can be finished in five minutes after the gelatin is melted.

ECZEMA SOLARE

RALPH H. SALSBERG, M.D., Newark, N. J.

On July 5, 1934, Mrs. B. R., aged 34, presented herself at my office with large erythematous patches on the face, neck and arms. There were several excoriations from scratching but no vesicles or bullae. The condition recurred each summer for the past eight years on exposure to the sun's rays and was accompanied by intense itching and burning. Treatment before had been without avail, and the patient had usually suffered throughout the summer. Examination of the urine for porphyrin [1] gave negative results. The patient was given a meat-free diet low in protein and dilute hydrochloric acid by mouth. She was also given for local appli-

1. Templeton, H. J., and Lunsford, F. C.: Eczema Solare and Porphyria, Arch. Dermat. & Syph. **25**:691 (April) 1932.

cation a cream containing quinine,[2] because of its fluorescence in the same manner as a light-sensitive skin and hence its absorption of ultraviolet rays. However, she found this uncomfortable to use and could not leave her home. I then gave her a lotion containing quinine hydrochloride, 15 per cent, zinc oxide, 5 per cent, and glycerin, 10 per cent, in rose water. She found this pleasant to use and effective, and for the first time was afforded protection and relief for the remainder of the summer. I have since used this lotion on patients with fair complexions whose skin burns easily on exposure to the sun, with excellent results.

23 Johnson Avenue.

2. Barber, H. W., and Howitt, F. C.: Some Observations on Light Sensitization, Guy's Hosp. Rep. **76**:314, 1926.

OINTMENT FOR PREVENTING SUNBURN

HERMAN SHARLIT, M.D., New York

My attention has recently been called to the fact that a simple procedure for preventing sunburn long used in this office is not generally known to dermatologists. Phenyl salicylate (salol) incorporated in a cream makes an effective topical application for absorbing ultraviolet rays and so preventing sunburn.

Phenyl salicylate is used in 10 per cent strength. The cream is made by dissolving the drug in a minimum amount of liquid petrolatum, and this solution is thoroughly dispersed in a cold cream base. Such a cream used on the surface of the skin in a thin layer by the usual manner of applying a cosmetic is sufficient to effect the desired result.

BLACK TONGUE

FRED WISE, M.D., NEW YORK

I have cured three patients with black, hairy tongue by the application of a 50 per cent solution of trichloracetic acid. In one case a single application sufficed; in the other two cases three applications at fortnightly intervals resulted in cure. The application gives rise to only slight discomfort, lasting five or ten minutes. In using the remedy, one should first wipe the affected area dry and then apply the solution by means of a cotton swab until the surface turns grayish white. My three cases occurred in men.

PYREX BOTTLES FOR STERILE SOLUTIONS

RUBEN NOMLAND, M.D., CHICAGO

I have found that 4 and 8 ounce pyrex nursing bottles plus the rubber slip-on covers, obtainable wherever the nursing bottles are sold, make excellent containers for material that may be sterilized by boiling.

Notices

PUBLICATION OF SOCIETY TRANSACTIONS

The ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY is getting into difficulties over Society Transactions. They are becoming so voluminous that unless some action is taken to limit them they will demand more space than can be given to them without crowding out other desirable material. There are, of course, more dermatologic societies sending in reports, but another reason is that it has become a custom to send in full descriptions and data of cases that present no unusual features. We have been compelled to omit a good many reports, because while they might contain well worked up reports of cases they present no points that are not familiar. We are therefore compelled to edit the transactions drastically.

Secretaries will assist us and make their reports more satisfactory if they will bear in mind the difficulties we are under and avoid giving unessential details of cases that present nothing new, whether they are familiar to one in textbook literature or from repeated reports of similar cases in current literature. If the reporter thinks it desirable that at least a record should be made of a case, he may note that, say, "Dr. John Smith presented a case of acanthosis nigricans."

CORRECTIONS

In the article by Dr. C. M. Hasselmann, entitled "Fatality from Exacerbation of Latent Tuberculosis Due to Thio-Bismol in a Case of Yaws," in the May issue (ARCH. DERMAT. & SYPH. **31**:686, 1935), an inferior "2" was omitted after each "H" in the formula for thio-bismol. The formula should therefore read:

$$\begin{array}{r} \diagup\ \text{S-CH}_2\text{-COO-Na} \\ \text{Bi} - \text{S-CH}_2\text{-COO-Na} \\ \diagdown\ \text{S-CH}_2\text{-COO-Na} \end{array}$$

In the article by Drs. M. E. Obermayer and S. W. Becker, "A Study of Crude Coal Tar and Allied Substances: Preliminary Report," in the June issue (*Arch. Dermat. & Syph.* **31**:796, 1935) "coal tar solution, N. F." in parenthesis following "liquor carbonis detergens," on page 797, should read: "crude coal tar."

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

MELANOTIC NEOPLASMS OF THE SKIN. S. W. BECKER, Am. J. Cancer **22**:17 (Sept.) 1934.

Becker differentiates melanoblasts from chromatophores and demonstrates that pigmentation in melanotic neoplasms is derived from melanoblasts, which are dendritic cells situated at the dermo-epidermal junction. These cells may be modified basal cells, but they appear more likely to be migratory cells of nervous origin, possibly derived from the sheath of Schwann. Chromatophores are phagocytic dermal cells of the upper dermis and papilla that carry pigment but do not produce it. Pigmented nevi are divided into two groups, the elevated, which contain nevus cells, and the nonelevated, which contain only an abnormal number of melanoblasts. Melanoblasts are not nevus cells. The latter are round, oval or polygonal with pale-staining nuclei and protoplasm, and they may contain pigment and give a positive dopa reaction as do melanoblasts and may have a similar origin. Malignant pigmented neoplasms may be of epidermal or mesodermal origin and are best designated as malignant melanoma instead of melanocarcinoma or melanosarcoma. In this grouping are included lentigo maligna and the nonpigmented variety of melanosarcoma. The melanotic neoplasms are differentiated from epitheliomas or carcinomas that contain melanoblasts as secondary factors. Becker believes the pigmented or melanotic epithelioma to be a benign epidermal neoplasm containing melanin. Evidence of melanoblastic proliferation is accepted as an indication that the lesion is already a malignant melanoma. Brown nevi and blue nevi apparently differ chiefly in that in the latter type of lesion the melanoblasts are all situated deeper in the derma, the interposition of connective tissue giving a blue color. Any preexisting melanotic lesion that shows peripheral extension should be regarded as malignant or potentially malignant.

FOERSTER, Milwaukee.

ACRODYNIA: REPORT OF A CASE WITH A PATHOLOGIC STUDY. WILLIAM C. DEAMER and GERSON R. BISKIND, Am. J. Dis. Child. **48**:1326 (Dec.) 1934.

In reporting a case of acrodynia with a fatal outcome Deamer and Biskind call attention to the elevation of the blood pressure which is sufficiently constant to be of real value in the differential diagnosis in doubtful cases. Tachycardia which is persistent is also of significance.

The authors made an unsuccessful attempt to induce the disease in a monkey by intracranial inoculation with the patient's spinal fluid and with a filtrate of the spinal cord.

Certain pathologic changes in the sympathetic nervous system and in the ganglions of the posterior roots are reported.

FISTULA AURIS CONGENITA. THEODORE K. SELKIRK, Am. J. Dis. Child. **49**:431 (Feb.) 1935.

The term fistula auris congenita refers to a small sinus of the external ear, which opens most commonly at the anterior border of the ascending limb of the helix. The clinical significance of such a fistula lies in the fact that it can give rise to an offensive discharge, form a retention cyst or become infected. Infection can give rise either to a lesion of the fistula itself or to a lesion of the face in front of the ear. Treatment of the latter type of lesion may be unsuccessful unless the origin in the congenital fistula is recognized.

Selkirk observed 172 cases of fistula located at the anterior margin of the helix. The condition is comparatively common, but it is easily overlooked. Nearly 1 per cent of white school children and about 5 per cent of colored school children presented this type of fistula.

Other types of aural fistulas are discussed. ANDERSON, Los Angeles.

SPONTANEOUS RUPTURE OF THE ESOPHAGUS IN SYPHILIS. W. E. GLASS and W. FREEMAN, Am. J. M. Sc. **189**:80 (Jan.) 1935.

In a series of 496 autopsies on patients with mental diseases, 2 cases were found in which death was due to rupture of the esophagus. This number was 40 per cent of the total number of patients who had died during paretic siezures.

The presence of syphilitic periarteritis, vascular occlusion, formation of scars and epithelial damage is the sequence responsible for the esophageal rupture. Both cases are reported in detail.

METASTATIC MELANOCARCINOMA WITH APPARENT RECOVERY. J. J. ELLER and I. L. SCHONBERG, Am. J. M. Sc. **189**:240 (Feb. 3) 1935.

In the case reported a recurrent growth occurred over the scapula soon after the first removal of a blue-black mole.

Metastasis occurred in spite of wide excision with electrocautery, and microscopic examination of the glands showed melanocarcinoma. Roentgen and radium irradiation and excision of lymph nodes were then employed and were followed by a flare-up of pigmented moles on other parts of the body. This flare-up subsequently receded without treatment.

No recurrence has been noted in four and one-half years in spite of the development on the left cheek of a melanocarcinoma which was removed surgically and did not recur. JAMIESON, Detroit.

THE CITOCHOL TEST FOR THE DIAGNOSIS OF SYPHILIS. K. DEISSLER and A. B. BAKER, Am. J. Syph. & Neurol. **19**:48 (Jan.) 1935.

The citochol test, one of the most popular flocculation tests for syphilis in European countries, is seldom used in the United States. Deissler and Baker compare this test with the Kahn and Wassermann tests. A brief description of the preparation of the citochol antigen and the technic of performing the test are given.

From the standpoint of sensitivity, specificity and practicability, the citochol test compares favorably with the Kahn test, and both proved to be superior to the Wassermann reaction. So far as the use of two serologic tests is advocated in the diagnosis of syphilis, the authors are of the opinion that the Kahn and citochol tests, because of their high degree of specificity and sensitivity and because of the simplicity of their technic, may well be the two methods of choice.

A COMPARATIVE ESTIMATION OF CEREBROSPINAL FLUID FROM CISTERNAL AND LUMBAR PUNCTURE IN SYPHILITIC PATIENTS. K. A. MOSKVIN, L. M. MARKUSS and V. N. VASSILIEVA, Am. J. Syph. & Neurol. **19**:77 (Jan.) 1935.

In a comparative study of cisternal and lumbar fluids from syphilitic patients little signicant variation in the Wassermann reaction was observed. The reaction to the colloidal and protein tests is more intensely positive and lymphocytosis is more marked in the fluid obtained from the lumbar region. Examination of cisternal fluid is a valuable adjunct to that of the cerebrospinal fluid in making a diagnosis of syphilis, particularly when lumbar puncture is contraindicated, when frequent examination of the lumbar fluid is impossible because of meningism and when the fluid cannot be obtained by lumbar puncture.

JUVENILE PARETIC NEUROSYPHILIS STUDIES. WILLIAM C. MENNINGER, Am. J. Syph. & Neurol. **19**:88 (Jan.) 1935.

This study is concerned with the typical complications, stigmas and endocrinopathies occurring in cases of juvenile dementia paralytica. Physical complications are rare, probably because the presence of severe syphilitic disease results in an early fatal issue in most cases of congenital neurosyphilis and because the patients literally do not live long enough to acquire dementia paralytica.

Stigmas of congenital syphilis are present in about 75 per cent of the patients; defective development of the teeth occurs in about 40 per cent; anomalies of bony development are found in more than 20 per cent, and ocular lesions, in 12.5 per cent.

The endocrinopathies seen associated with juvenile dementia paralytica are ill defined. Body infantilism is recorded in about 20 per cent of the cases. Genital hypoplasia occurs in about 30 per cent of the cases in males, and menstruation either never develops or ceases in about 25 per cent of those in females. Clearcut pituitary dysfunction, usually hypopituitarism, is manifest in a few cases. Disturbances of thyroid function appear to be an occasional accompaniment of juvenile dementia paralytica.

REUTER, Milwaukee.

TULAREMIA: A CONSIDERATION OF ONE HUNDRED AND TWENTY CASES WITH OBSERVATIONS AT AUTOPSY IN ONE. C. N. KAVANAUGH, Arch. Int. Med. **55**: 61 (Jan.) 1935.

A brief history of tularemia is given together with a discussion of the symptomatology, distribution, incidence, immunity, contagion and bacteriology. Kavanaugh classifies the types of infection as primary cutaneous tularemia, primary ophthalmic tularemia and cryptogenetic tularemia (typhoid type), the last being the type usually found in laboratory workers.

The usual symptomatology is described fully (primary cutaneous lesion, subcutaneous nodules, fever, etc.).

In twenty-three cases a cutaneous eruption was noted which appeared during the second or third week and lasted from a few days to three or four weeks. The type of lesion varied, being macular, papular, vesicular or pustular or presenting any combination of transitional forms. The eruption occurred most frequently on the arms and necks; it was always bilateral and usually symmetrical.

Emphasis is laid on bearing in mind the possibility of tularemia as a diagnosis in any part of the country where the disease may be found. The intradermal test is the earliest available diagnostic aid in determining the presence of a tularemic infection. Agglutinins do not appear in the blood during the first week of the disease but are found during the second week, and in no tested case have they been found to disappear entirely even years afterward.

In the series reported on there was a mortality of 4 per cent.

Prophylaxis by education of the public and preventive inoculation are both valuable in preventing the spread and development of the disease among those most liable to acquire the infection.

Symptomatic treatment, incision of suppurating glands, etc., constitute the usual treatment routine; the primary lesion, however, should not be incised. In some cases goat antiserum has been effective.

JAMIESON, Detroit.

CAMOMILE (ANTHEMIS COTULA) AS A SKIN IRRITANT. A. H. ROWE, J. Allergy **5**:383 (May) 1934.

The author directs attention to the fact that Anthemis cotula is a common irritant of the skin. Patch tests made with the dried plant produced definite erythematous and vesicular reactions in nearly all of the children and the adults in his series within twenty-four hours. Infants in the first few days of life showed no reaction. The specific reacting substance is an oil or resin.

EXPERIMENTAL STUDY OF THE ETIOLOGY OF DERMATITIS VENENATA. H. W. STRAUS, J. Allergy **5**:568 (Sept.) 1934.

Sensitization of the skin to poison ivy was attempted in ten new-born infants by oral administration of an alcoholic extract of poison ivy and in ten others by subcutaneous injection of the extract. No sensitization occurred in the feeding experiment, and only one infant was sensitized by injection. In the latter case the possibility of accidental contact of the extract with the epidermis could not be excluded.

Application of a paste containing poison ivy to the skin resulted in successful sensitization of 72.9 per cent of forty-eight new-born infants. The infants who gave positive reactions to poison ivy also gave positive reactions to poison sumac, showing that the active principles of the two plants are immunologically identical.

CARO, Chicago.

STUDIES ON ANAPHYLAXIS WITH POLLEN. C. BERNSTEIN JR., J. Exper. Med. **61**:149 (Feb.) 1935.

In these experiments it was shown that guinea-pigs which received injections of small doses of the pollen extract of burweed marsh-elder did not show any evidence of anaphylactic shock when receiving the same kind of pollen three weeks later. In animals, however, which had been sensitized with horse serum either before or at the time they received injections of pollen the pollen extract alone produced shock after three weeks.

FURTHER STUDIES ON KALA-AZAR: LEISHMANIA IN NASAL AND ORAL SECRETIONS OF PATIENTS AND THE BEARING OF THIS FINDING ON THE TRANSMISSION OF THIS DISEASE. C. E. FORKNER and LILY S. ZIA, J. Exper. Med. **61**:183 (Feb.) 1935.

Examination of material from twenty-two patients proved to have kala-azar showed typical parasites in the nasal secretions of twelve patients and in three smears made from pharyngeal tonsils.

The authors discuss in detail the question of transmission of Leishmania by means of sand-flies and also that of transmission by direct and indirect contact. While definite proof is lacking regarding the natural mode of infection, they believe that their arguments support the theory of transmission by direct or indirect contact.

MALIGNANT DISEASE IN NATIVES OF NIGERIA: AN ANALYSIS OF FIVE HUNDRED TUMORS. E. C. SMITH and B. G. T. ELMES, Ann. Trop. Med. **28**:461 (Dec. 20) 1934.

In discussing malignant disease among Africans, Smith and Elmes note the varying opinions regarding its frequency but express the belief that there is no real scarcity of malignant disease among these persons. Sarcoma and carcinoma comprised 89 per cent of the cases; a few rarer types, such as tumors of the parotid region, endothelioma, adamantinoma, cylindroma, perithelioma, teratoma and chorionepithelioma, made up the remaining 11 per cent. Seventy squamous cell carcinomas were found; this number constituted 14 per cent of the total number of tumors.

Of the forty melanotic sarcomas, thirty had their origin in the foot, suggesting injury as the exciting factor.

Ten Kaposi sarcomas (2 per cent) were noted in this series. Other tumors occurred in various parts of the body—in the breast, viscera, bones, glands, etc.

A number of excellent illustrations and photomicrographs showing types and locations of growths rarely seen at present accompany the article.

A Note on the Staining of Mycobacterium Leprae in Tissue Sections. J. Lowe, Indian J. M. Research **22**:313 (Oct.) 1934.

Lowe gives in detail a method of staining leprous tissue which is useful when it is more essential to stain for bacteria than for good differentiation of the cells. By this method bacilli are often shown to be numerous in cases in which other methods had shown few or no lepra bacilli.

Cutaneous Leishmaniasis as a Natural Infection of a Dog in India. J. A. Sinton and H. E. Shortt, Indian J. M. Research **22**:393 (Oct.) 1934.

Infection with Leishmania occurred about the nose of a dog. The case is recorded on account of the rarity of such an occurrence in India.

Ulcerative Granuloma of the Pudenda Treated with Intravenous Injections of Tartar Emetic [Antimony and Potassium Tartrate] and a Dusting Powder Containing Mild Mercurous Chloride and Antimony Oxide. Necrotic Colitis. Death. J. Burton Cleland, J. Trop. Med. **37**: 371 (Dec. 1) 1934.

A male Australian aboriginal had had a typical ulcerative pudendal granuloma involving the penile and inguinal region. This ulceration had progressed for three years.

Treatment consisted of intravenous injections of antimony and potassium tartrate and local treatment with a dusting powder containing equal parts of antimony oxide, mild mercurous chloride and zinc oxide. Toxic symptoms developed a few days later, and death followed in one month. An intense necrotic colitis was found on autopsy, presumably due to the mild mercurous chloride or the antimony, although chemical examination of the colon and its contents revealed no antimony, arsenic or mercury.

Creeping Eruption at the Natal Coast. F. G. Cawston, J. Trop. Med. **37**: 374 (Dec. 1) 1934.

Domestic pets of Durban are commonly infested with the hookworm, Ancylostoma braziliense, which is also the cause of sandworm disease and of creeping eruption in America.

The treatment in Durban consists of soaking the part in diluted compound solution of cresol for thirty minutes and then attempting to penetrate the skin by fumes of ether or by the application of carbon dioxide snow. Some of the native remedies prepared from fresh leaves and crushed roots have been of greater value than standard measures.

A Note on the Use of Tinfoil in the Treatment of Abrasions and Ulcers. J. A. Carman, J. Trop. Med. **37**:376 (Dec. 1) 1934.

Many tropical ulcers are the result of superficial abrasion and secondary infection. As dressings of gauze are liable to stick and be difficult to remove, Carman has used tin-foil obtained from a package of cigarets to cover over the abraded or infected area after the ulceration has been thoroughly disinfected. These dressings do not have to be removed oftener than every few days; they do not adhere to the edges of the wound, and granulation takes place readily and rapidly under the tin-foil.

Elephantiasis in South Africa and Basutoland. F. G. Cawston, J. Trop. Med. **38**:34 (Feb. 1) 1935.

In a short article Cawston emphasizes the necessity of examining the blood at night in all cases in which the presence of microfilariae of elephantiasis is suspected. Sporadic cases unrelated to microfilarial infection are rare.

Antimony is the only drug that seems to promise a cure, but complete courses of antimony and potassium tartrate are necessary. Jamieson, Detroit.

THE NATURE OF "GLOSSITIS RHOMBICA MEDIANA." H. O. LOOS and L. HÖRBST, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **138**:122 (May 17) 1934.

Loos and Hörbst studied the condition of the tongue characterized by a rhombus-shaped, reddened, sharply demarcated lesion lying medially in the middle third of the tongue and named by Lane "glossitis rhombica mediana." Heretofore the origin and nature have been uncertain. They examined histologic sections (removed under local anesthesia) in eight cases. Microscopic observation showed a definite similarity of all of these. A marked widening and thickening of the involved epithelium were seen. In the upper layers were numerous nucleated horn cells with keratohyaline granules. Often the hornifications were in a sphere-shaped form. In all cases the absence of taste papillae was the same. The epithelium also show a small amount of leukocytic and lymphocytic infiltration. One case differed from the others in that mitotic figures were visible in the epithelium. The submucosa was rich in widened blood and lymph vessels of different sizes. The larger blood vessels were thin-walled and delicate. The lumen was sometimes empty and sometimes filled with erythrocytes. In one case the deeper vessels showed sinus-like widening. In the neighborhood of the capillaries were small agglomerations of round cells and plasma cells, which were also present in small numbers in the connective tissue. Also near the larger vessels were collections of round cells and leukocytes which decreased in number in the deeper layers of the lower mucosa. The most important observations in all cases were the absence of taste papillae, the epithelial hypertrophy and the increase and widening of the blood and lymph vessels in the submucosa. These observations place the so-called "glossitis rhombica mediana" in the group of vascular nevi. The localization of the embryonal anlage of the tuberculum impar allows it to be placed in the group of fissured angioma. Evidences of chronic inflammation such as the changes in the epithelium are explained as secondary and due to chronic irritation of the faulty and functionally inferior tissue.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

IS THERE A CONNECTION BETWEEN THE RESULTS OF PATCH TESTS OF JADASSOHN AND BLOCH AND FEVER AND SWEATING? W. ENGELHARDT and W. MAHLER, Dermat. Wchnschr. **99**:1205 (Sept. 15) 1934.

Engelhardt and Mahler were able to demonstrate that patients showing an elevation of temperature and increased sweating were more sensitive to external irritants applied in patch tests. When there was increased sweating without elevation of the temperature the effect was not noticeable.

FORMATION OF MULTIPLE MALIGNANT TUMORS FOLLOWING CHRONIC ACRODERMATITIS ATROPHICANS. HANS-HEINZ SEYFERT, Dermat. Wchnschr. **99**:1234 (Sept. 22) 1934.

Seyfert reports on two patients: The first patient had acrodermatitis atrophicans of seven years' duration. A number of tumors developed one of which was excised and was found to have the histologic picture of sarcoma. In the second patient three squamous cell epitheliomas developed after the acrodermatitis.

RESEARCHES IN THE FIELD OF PSORIASIS VULGARIS: I. INFLUENCE OF ULTRAVIOLET RAYS ON ARTIFICIALLY PRODUCED LESIONS OF PSORIASIS. L. N. MASCHKILLEISSON and L. A. ABRAMOWITSCH, Dermat. Wchnschr. **99**:1240 (Sept. 22) 1934.

The authors used eleven patients with psoriasis as material for this series of experiments. Köbner's phenomenon (the production of a psoriatic lesion as the result of a scratch on the normal skin of a patient with psoriasis) was positive in all the patients. In seven of them equal scratches were made on the right and left forearms; the one forearm was exposed to ultraviolet radiation on alternate days for three doses while the other was untreated. The effect of the irradiation was to increase the rate of the reaction so that the artificially produced psoriatic

lesion was disappearing by the time the control area showed a reaction. In the remaining four patients one arm was irradiated on three alternate days before the scratch tests were performed. The psoriatic response was slower and more persistent on the irradiated side.

PUSTULOSIS VACCINIFORMIS ACUTA IN AN ADULT. HANS J. SCHMITZ, Dermat. Wchnschr. **99**:1267 (Sept. 29) 1934.

In a 30 year old man who had had eczema since infancy a vacciniform eruption developed over the greater part of the body. There was no history of exposure to smallpox. The condition was fatal.

STUDIES ON THE RESISTANCE TO BREAKING OF HUMAN HAIR. ALFRED MARCHIONINI and HERBERT ARETZ, Dermat. Wchnschr. **99**:1285 (Oct. 6) 1934.

An apparatus was constructed to determine the weight which a length of hair can hold before breaking. Samples from persons with hair of various colors were tested, the hairs being taken from the scalp, pubes and axilla of each person. Considerable individual variation was noted, but in each instance the axillary hair was found to be weaker than the other two specimens. Soaking the hair for three hours in water increased its strength somewhat. This increase in strength was especially noticeable in the case of the axillary hair, the strength of which practically equaled that of the other two types of hair after soaking. The difference in strength may be due to the washing away of the alkaline secretions of the axilla.

DIFFERENCE IN THE PIRQUET REACTION ON THE TRUNK AND ON THE LIMBS. HELMUT RACKWITZ, Dermat. Wchnschr. **99**:1290 (Oct. 6) 1934.

By tests on a series of cases Rackwitz shows that the Pirquet reaction is more frequently positive when the inoculation is made on the trunk (abdomen or chest) than when it is made on the arm or leg. A considerable number of persons who showed a positive Pirquet reaction on the trunk and a negative reaction on the limbs had stigmas of disturbance of the vegetative system, especially acro-asphyxia.

PIGMENTATION OF THE NAILS DUE TO THE ACTION OF LIGHT FOLLOWING IMPREGNATION WITH MERCURY. A. STÜHMER, Dermat. Wchnschr. **99**:1316 (Oct. 13) 1934.

Stühmer shows that the pigmentation of the finger-nails due to the application of a solution of corrosive mercuric chloride or of an ointment of ammoniated mercury does not occur unless the nails are exposed to light. When pigmentation does occur it involves the thickness of the nail, as can be shown by scraping the nail.

NAEVUS SYRINGOCYSTADENOMATOSUS PAPILLIFERUS. J. DÖRFFEL, Dermat. Wchnschr. **99**:1318 (Oct. 13) 1934.

A 14 year old girl presented on the cheek a small mass consisting of a group of small nodules. It had been present since birth and had increased gradually in size by the development of new nodules. Histologic examination showed a syringocystadenoma. The findings are discussed in detail.

A CASE OF PRINGLE'S DISEASE WITH CHANGES IN THE EYEGROUNDS AND IN THE MUCOSA OF THE BLADDER AND RECTUM. E. KUCHENMEISTER, Dermat. Wchnschr. **99**:1333 (Oct. 13) 1934.

A typical case of adenoma sebaceum of the Pringle type is described. In the walls of both the bladder and the rectum numerous small shiny nodules, clinically diagnosed as fibromas, were observed. The eyegrounds also showed small tumor-like growths.

Dermatitis Exfoliativa Generalisata Chronica (Wilson and Brocq). Hans Säuferlin, Dermat. Wchnschr. **99**:1337 (Oct. 13) 1934.

A patient, aged 45, had generalized exfoliative dermatitis which was fatal after a period of one and one-half years. Physical examination and necropsy failed to reveal any etiology for the cutaneous condition. Säuferlin expresses the belief that this case is an example of a true primary erythroderma.

The Treatment of Boeck's Sarcoid with Esters of Chaulmoogra and Hydnocarpus Oil. Sven D. Lomholt, Dermat. Ztschr. **70**:57 (Oct.) 1934.

A mixture of the ethyl esters of various unsaturated fatty acids of chaulmoogra and hydnocarpus oil may be given either intramuscularly or intravenously. Twelve patients with typical sarcoid of Boeck were treated with this preparation. Eight of them were practically cured, and in the remaining four marked improvement resulted. In some instances rather severe reactions occurred. The intramuscular injection of the drug was at least as effective as the intravenous injection except for the pain and occasional formation of abscesses. In one case granuloma annulare responded rapidly to this treatment. The injections practically always caused marked eosinophilia, which receded gradually and occurred again when subsequent injections were given.

Taussig, San Francisco.

Elimination of Chlorides in Pemphigus and in Other Exudative Dermatoses. Marie Runtová, Česká dermat. **15**:145, 1934.

The study includes fourteen cases of pemphigus, two of dermatitis herpetiformis and fourteen of other exudative dermatoses. Tests on fourteen controls gave normal values for the chloride content of the bullae (from 0.5 to 6 per cent), of the serum and of the blood (from 0.4 to 0.5 per cent). A decided retention of chlorides was found in more than 50 per cent of the cases of pemphigus; the retention was most pronounced in severe cases and in those which ended fatally. One case of malignant pemphigus vegetans particularly demonstrated a definite relation between the fluctuating severity of the symptoms and the amount of salt retained. During the remission, the values for chlorides approached the upper normal limit (0.601 per cent); when a new crop of lesions appeared the figure for retention rose to 0.84 per cent, and it rose to 0.85 per cent just before the patient died.

Having reviewed various theories as to the significance of chloride retention and its relation to the defense mechanism of the system, Runtová advances Šamberger's view that a higher concentration of chlorides may increase the resistance against pyogenic infection. Cases of pemphigus show little tendency to pyogenic complications such as are frequently seen in cases of exfoliative postarsphenamine dermatitis, weeping eczema, etc.

An Attempt at Etiologic Treatment of Mycosis Fungoides. Karel Hübschmann, Česká dermat. **15**:154, 1934.

Hübschmann considers mycosis fungoides as a specific inflammatory process rather than as a reaction of the sarcoid type and points out a certain analogy between mycosis and other specific granulomas such as syphilis, tuberculosis and some tropical dermatoses. Because of this he attempted to ascertain whether the drugs successfully used in those diseases were helpful also in cases of mycosis fungoides. Copper and tin salts of gynocardiac acid were used in one series of injections and gold preparations and fuadin in another. Both types of treatment seemed to have some favorable effect on the cutaneous condition. Germanin had a remarkable tonic effect on the general condition of the patient. Hübschmann does not express his preferences for and does not discuss the relative values of the preparations used.

LOEWENSTEIN'S METHOD OF CULTIVATING TUBERCULOSIS BACILLI IN TUBERCULOSIS OF THE SKIN. J. FRIEDMANN and J. KISEL, Česká dermat. **15**:160, 1934.

Loewenstein's method of cultivating tuberculosis bacilli from circulating blood was used with negative results in forty-two cases of cutaneous tuberculosis including thirty-two cases of lupus vulgaris, four of lupus erythematosus, three of scrophuloderma, two of tuberculosis cutis and one of tuberculosis oris. In four cases positive results were obtained when excised lesions were planted on Loewenstein's medium: In three of nine cases of lupus vulgaris and in one case of tuberculosis oris the cultures were positive for tubercle bacilli. A part of the excised lesions was also planted in Besredka's bouillon and inoculated into guinea-pigs. Besredka's bouillon gave the same positive results, but the growth appeared three weeks later than on Loewenstein's medium. Biologic tests on guinea-pigs were negative in all the cases in which negative cultures had been obtained and also in two of four cases in which the positive cultures had resulted.

EXTENSIVE HERPES ZOSTER WITH CHANGES IN THE CEREBROSPINAL FLUID IN A CASE OF SECONDARY SYPHILIS. KAREL HÜBSCHMANN, Česká dermat. **15**: 164, 1934.

Herpes zoster appeared during the first course of combined treatment after the fifth injection of a preparation containing arsenic and after the sixth injection of one containing bismuth. The spinal fluid was under normal pressure, and examination of the fluid showed 16 small lymphocytes, 1 polymorphonuclear, an increased amount of globulin and a negative Wassermann reaction (Bordet's modification of the Wassermann test). The curve for gold chloride was of the acute meningeal type. Hübschmann ascribes the changes in the fluid to the herpes zoster rather than to syphilis.

LOEWENSTEIN'S METHOD OF CULTIVATING KOCH BACILLI. F. KOGOJ and A. ZUK, Česká dermat. **15**:177, 1934.

At the hygiene institute in Zagreb, Loewenstein's method of cultivating Koch bacilli from circulating blood was used in seventy-one cases, including twelve cases of tuberculosis of the skin or mucous membranes and seven of lupus erythematosus. All the cultures gave negative results. Several positive results were obtained by this method on the blood of guinea-pigs and of rabbits inoculated with human and bovine types of Koch bacilli.

EPICUTANEOUS REACTION TO TUBERCULIN. M. SCHWARZWALD, Česká dermat. **15**: 188, 1934.

Patch tests with 10 and 50 per cent solution of old tuberculin gave negative results in forty of forty-three cases of lupus vulgaris. The reactions were more intense and more often accompanied by marked infiltration of surrounding tissues than those which appeared in the control cases. The first control group consisted of cases of pulmonary, surgical and osseous tuberculosis. In seventeen cases of osseous tuberculosis in children the tests were all positive. In twenty-nine cases of pulmonary tuberculosis there was only one negative reaction. (The patient who showed the negative reaction also showed anergy and a negative reaction to the Mantoux test.) Schwarzwald's results, therefore, differ from those of Nathan and Kallós who obtained negative reactions to patch tests in all their cases of pulmonary tuberculosis. In the second group of twenty-one purely dermatologic cases there were nine positive reactions; these were mostly weak and delayed. The last group consisted of forty patients with normal skin and without any clinical manifestations of tuberculosis; eighteen of these showed positive reactions. In the majority of cases the Pirquet test and the epicutaneous test gave the same results.

SPINKA, Texarkana, Texas.

CUTANEOUS TESTS BY MEANS OF COLORING MATTER. S. L. KWIATOWSKI, Przegl. dermat. **29**:237 (June) 1934.

In his experiments Kwiatkowski tried to ascertain the influence of intradermal injection of a stain on cutaneous reactions caused by inflammation, allergy and histamine. He used the method of Leszczyński employing a 0.2 per cent solution of trypan blue, which, when injected intradermally, produces a round or slightly oval blue ring.

The author made the following observations: The intradermal injection of trypan blue did not influence the course or the intensity of the inflammation of the skin. The inflammatory process inhibited the formation of the colored ring only in some cases. In most cases the trypan blue exerted no influence on the histamine reaction. In some instances the histamine reaction was partly inhibited; rarely there was complete inhibition. In most cases the allergic reaction produced by vaccine and particularly by gonococcus vaccine was not inhibited when these substances were injected some time after the intradermal injection of trypan blue. Also when the allergic reaction was produced before the injection of trypan blue no inhibition of the reaction took place. In the latter case it was noticed in some instances that the allergic reaction was able to block the penetration of the stain.

Kwiatkowski explains the different results obtained on the basis of different conditions of the cells of the reticulo-endothelial system. He considers the cutaneous reaction by means of coloring wheals suggested by Leszczyński as a new vital staining method which will help to explain many facts relating to the physiology and pathology of the reticulo-endothelial system of the skin.

CHANGES IN THE BLOOD AND THE FUNCTIONS OF THE SKIN IN ECZEMA. S. FEDOSEWICZ, Przegl. dermat. **29**:270 (June) 1934.

In a study on thirty cases of eczema Fedosewicz made the following observations regarding the changes of the blood picture and the reactions of the skin to different substances: In nearly all the cases there was a shift of the leukocyte formula to the left, the index varying from 0.09 to 0.33. Eosinophilia and lymphocytosis predominated; monocytosis was more rarely observed, and in one case monocytopenia was present. The percentage of hemoglobin was frequently low. Fedosewicz carried out on the same patients intradermal tests with physiologic solution of sodium chloride, sterilized milk, staphylococcus and streptococcus vaccine, tuberculin solution and two proprietary preparations. He read the reactions half an hour, twenty-four and forty-eight hours after the injection. With the exception of eleven negative reactions to physiologic solution of sodium chloride and two negative reactions to sterilized milk all the reactions were positive, the intensity of the reaction depending on the agent used. In comparing the reactions produced by the staphylococcus and streptococcus vaccine it was found that in the majority of cases the former produced a much stronger reaction than the latter. No proportionate relation was noted between the intensity of cutaneous reaction and the number of eosinophils or monocytes in the blood. The cutaneous reactions which appeared late were much stronger than those which appeared early. In two cases in which the early intradermal reaction was the stronger there was noted a weak humoral manifestation of the allergic process; the leukopenia and lowering of the blood pressure were only of slight degree.

BLOOM, New York.

Society Transactions

SAN FRANCISCO DERMATOLOGICAL ASSOCIATION

JOHN M. GRAVES, M.D., *Secretary*

Sept. 28, 1934

L. R. TAUSSIG, M.D., *President*

ACNE AGMINATA. Presented by DR. ERNEST K. STRATTON.

H. W., a woman aged 47, consulted me in June of this year regarding a chronic inflammatory papulopustular eruption of five months' duration, involving the greater part of the face. There was a tendency to grouping about the chin, malar prominences and supra-orbital ridges. The lesions were purplish; many of them were discrete and capped with yellowish pustules.

In November 1933 the patient had an acute attack of bronchial asthma and received many intravenous injections of a combination of epinephrine and pituitary gland used in bronchial asthma. She had taken iodides by mouth over a year ago. Many years ago she underwent a bilateral salpingo-oophorectomy on account of a tuberculous condition.

Roentgen examination of the chest showed evidence of a past infection about the roots of the lungs but no evidence of active pulmonary tuberculosis. Direct smears were negative for acid-fast organisms and showed some gram-positive streptococci. The results of a biopsy were as follows: In the corium there were multiple tubercles, some composed only of epithelioid cells and others of giant cells. A lymphocytic reaction surrounded the groups of tubercles. A section stained with carbolfuchsin did not reveal acid-fast organisms. Inoculation of guinea-pigs, however, gave positive results for tuberculosis.

The patient has improved remarkably on a salt-free diet, internal administration of calcium gluconate, inunctions of cod liver oil and treatment with ultraviolet rays from a water-cooled quartz mercury vapor arc lamp at weekly intervals.

DISCUSSION

DR. HARRY E. ALDERSON: I think that Doctor Stratton is obtaining good results, and the treatment he has been carrying out seems, in this case, to give the most promising results.

DR. H. J. TEMPLETON, Oakland, Calif.: After a hurried inspection I should have diagnosed this patient's eruption as acne rosacea. This case reminds me of a remark by Fuhs, that many reports of favorable therapeutic results following the roentgen treatment of acne rosacea are due to the fact that in many cases the condition is in reality acne agminata. One should examine microscopic sections of such lesions more frequently.

DR. N. N. EPSTEIN: I think it ought to be pointed out that the pathologic picture of a lesion of acne is not unlike that of a tuberculous lesion; both show the presence of giant cells.

TUBERCULID? Presented by DR. L. R. TAUSSIG.

W. B., a man aged 26, has an eruption which appeared two years ago after a severe attack of pleurisy. On the anterior surface of the left leg, midway between the knee and the ankle, is an oval atrophic scar about 3 cm. long. Below this area are numerous mahogany-colored follicular lesions. There are three or four coin-sized groups of follicular pigmented spots, confluent in the central portion, located below the scarred area. Over the outer malleolus is an erythematous,

slightly verrucous area about 8 cm. in diameter. There are a number of small ulcers in this area.

DISCUSSION

DR. L. R. TAUSSIG: The tentative diagnosis is tuberculid. The patient states that the eruption started about nine months after he had been confined to bed owing to what was apparently a tuberculous condition of the lung. He is presented for suggestions as to treatment and diagnosis.

DR. A. E. INGELS: I agree with Dr. Taussig that the lesion may be tuberculous; probably it is tuberculosis verrucosa cutis. However, I should like to emphasize the similarity to blastomycosis and bromoderma. A biopsy would give some information.

DR. H. E. MILLER: It is of interest that Dr. Taussig ruled out Majocchi's disease because of the unilateral distribution. I think that a unilateral tuberculid of the lower portion of the leg would also be unusual. The lesion seems to resemble a manifestation of true tuberculosis more than a toxic tuberculid.

DR. H. J. TEMPLETON, Oakland, Calif.: Two questions come to my mind: 1. If one diagnoses this lesion as a tuberculid until a biopsy is made, would it not be wise to make cultures to rule out coccidioidal granuloma? 2. Has the patient taken any bromides?

LYMPHOBLASTOMA? Presented by DR. FRANCIS TORREY.

Mr. A., a man aged 67, has a generalized exfoliative dermatitis with marked hyperpigmentation and severe pruritis. The past history is irrelevant except that an area of eczema has appeared on the neck every spring for twenty years, lasting about three months each time.

The present condition began eleven months ago with a furuncle on the scrotum and perineal pruritus; the erythema spread along both legs. There is no history of medication or of contact with chemicals.

The patient is well developed; his entire skin is lichenified, is from copper-colored to chocolate brown and shows exudation and fissures; the palms and soles are hyperkeratotic. There is generalized lymphadenopathy, the lymph nodes being firm and ranging in size from that of a pea to that of a hazelnut. The peripheral vessels are sclerotic. The blood pressure is 180 systolic and 75 diastolic, and there is a low whistling systolic murmur at the apex, transmitted to the left axilla.

The blood count showed 78 per cent hemoglobin, 4,190,000 red cells, 9,550 white cells, 62 per cent polymorphonuclears, 10 per cent eosinophils, 21 per cent lymphocytes, 1 per cent basophils and 6 per cent monocytes. Other laboratory examinations gave negative results. Roentgen examination showed no evidence of a mediastinal tumor.

Biopsy of a lymph node showed a chronic inflammatory process with a considerable deposit of brown pigment which did not stain with prussian blue.

Biopsy of the skin showed a moderate infiltration of lymphocytes and fibroblasts in the cutis, a reaction compatible with either an eczematoid process or lymphoblastoma, but the epidermis showed little pathologic change and no change characteristic of eczema.

DISCUSSION

DR. FRANCIS TORREY: The eruption is regarded as an exfoliative dermatitis belonging to the lymphoma group because of the generalized adenopathy, although the blood picture did not indicate this diagnosis. The biopsy showed a rather sharply demarcated infiltration of cells below the epidermis, which could fit in the picture of lymphoma or eczema, whereas the epidermis showed much less of the change which would have occurred if the eruption were eczematoid.

DR. L. R. TAUSSIG: This patient presents a picture which my co-workers and I have become accustomed to associate with diseases of the lymphoblastoma group. We have discussed similar cases with pathologists, on the one hand, and with clinicians, on the other, and often they do not agree with our diagnosis. In a certain percentage of the cases our diagnosis has been verified by the course of the

disease. Sometimes the disease turns out to be something quite different from the original diagnosis. In this case I doubt whether at this time either the pathologists or the clinicians would be willing to diagnose the condition as belonging to the lymphoblastoma group.

DR. H. E. MILLER: I believe that this man, like many patients with similar disorders, who were presented, will go along for a half-dozen years and then will die in spite of all therapy. I venture to say that if an autopsy is performed, it will show that little more is known about the classification of his disease than is known at present. In one case that I recall, twenty-three separate glands were taken out at autopsy and sectioned; only one showed the typical picture of Hodgkin's disease; the other twenty-two showed nothing unusual.

DR. A. E. INGELS: I think the patient's skin showed interesting features. It was darkly pigmented. One would suspect the patient of being of Negro origin. None of the sections showed a deposit of pigment. I should like to have an explanation as to the pigmentation. It is a striking clinical feature.

DR. H. J. TEMPLETON: Could not the pigmentation be explained on the same basis as in vagabond's disease, namely, as due to scratching, hemorrhage into the skin and escape of hemosidérin?

LYMPHOBLASTOMA (LYMPHATIC LEUKEMIA?). Presented by DR. N. N. EPSTEIN.

Mrs. C. D., aged 57, was first seen on Nov. 21, 1933. She complained of an intensely pruritic eruption of two years' duration involving almost the entire skin. The hands, forearms and legs were more severely affected than the other parts. In these areas there were considerable thickening and general erythema of the skin. Many areas were scaly and excoriated. The superficial lymph nodes were not markedly enlarged.

General examination gave essentially negative results except for hypertension, the blood pressure being 195 systolic and 110 diastolic. The spleen was not felt. The Wassermann and Kahn tests of the blood and examination of the urine gave negative results. Examinations of the blood showed:

	Nov. 21, 1933	Sept. 27, 1934
Hemoglobin	85 per cent	100 per cent
Red cells	4,170,000	4,970,000
White cells	16,000	27,750
Polymorphonuclears	41 per cent	42 per cent
Eosinophils	1 per cent	5 per cent
Lymphocytes	57 per cent	49 per cent
Monocytes	1 per cent	2 per cent
Myelocytes		2 per cent

A biopsy of the skin disclosed an exudate of inflammatory cells in the corium. The diagnosis based on the biopsy was: probably lymphoblastoma.

DISCUSSION

DR. N. N. EPSTEIN: This patient seems to have a lymphatic leukemia rather than lymphosarcoma. The percentage of polymorphonuclear leukocytes has remained low: 42 per cent. The rest of the white cells are essentially lymphocytes. Some relief followed the internal administration of a solution of potassium arsenite.

DR. HARRY E. ALDERSON: Some time ago Dr. Stratton made a valuable suggestion, namely, that small doses of amytal will relieve the itching. I have found this treatment to be of considerable use; ¼ grain (0.048 Gm.) is given every five hours.

DR. C. E. SCHOFF, Sacramento, Calif.: It seems to me that Dr. Epstein's patient shows a great deal more erythema than did Dr. Torrey's patient, regardless of the pigmentation in the skin of the latter. Dr. Epstein's patient has many fine scales, and I wonder whether his condition could be pityriasis rubra of Hebra.

DR. N. N. EPSTEIN: When the patient was first seen her eruption was scaly.

DR. E. K. STRATTON: The blood of Dr. Epstein's patient showed a leukemic trend.

DR. H. J. TEMPLETON, Oakland, Calif.: Not on the basis of my own experience, but rather from a review of the literature, it appears that the different kinds of lymphoblastoma may merge into one another. A condition may begin as lymphatic leukemia and end up as lymphosarcoma. The modern belief of the Viennese school is that pityriasis rubra of Kaposi is simply a type of lymphoblastoma.

LYMPHOSARCOMA. Presented by DR. A. E. INGELS.

C. R. P., aged 28, is a grocery clerk. He is married, and his wife and child are both well. He is apparently in good health. He presents on the volar surface of the left forearm one irregular lesion which consists of a granulating ulcer 3 by 4 cm. in diameter, fairly well defined and raised from 2 to 3 cm. over the surface. The ulcer is covered with a seropurulent exudate. There are no sinuses. The granulating tissue is semielastic to touch and has no sharp limitations in the subcutaneous tissue. Irregularly in the periphery there is a zone of surrounding scar covered with glossy, shiny epidermis which fuses irregularly into normal epidermis. Both the scar and the granulating ulcer have a fresh fleshy color. Two pigmented scars 1 cm. in diameter, residua of involuted tumors, can be seen on the forearm. There are no other scars or areas of pigmentation.

The anterior deltoid region and the region adjacent to the gluteal folds present a multipapular rash of a fresh deep red color. The papules are slightly raised over the surface, vary in size from 2 to 5 cm. in diameter, are slightly infiltrated and extend into the superficial portion of the cutis. They have a shiny, smooth, dry surface. The papules are discrete and are not painful when touched.

There is a tender swollen gland in the left axilla. It does not fluctuate. In the other axilla and scattered over the neck and inguinal regions are a few small discrete indolent glands.

The physical examination revealed no pertinent facts except that the tonsils have been removed.

The patient was seen at the office on April 9, 1934. Two months previously he had returned from Hawaii, where for six years he had been in the grocery business. He states that he has no syphilitic infection. He had a gonococcic infection six years ago, which healed promptly. The lesions started in November 1933 with a papular rash similar to the one now present in the gluteal area. The patient was then treated for scabies. This rash has persisted. In February, while he was still in Hawaii, two subcutaneous nodules developed on the left forearm, and shortly after a third nodule appeared higher on the forearm. They all increased slowly in size and finally broke down, forming granulating, crater-like ulcers covered with pus. The largest one has been open since, except between May and June, when it healed for one month. The other two healed with pigmented scars shortly after. None of the lesions presented sinuses.

Shortly after the tumors on the arm involuted, intradermal and subcutaneous tumors developed along the left arm, on the neck and on the upper part of the chest and back. In addition, a rash somewhat resembling an eruption of secondary syphilis appeared on the face, neck and upper portion of the chest. Except for the two aforementioned lesions, the tumors involuted after one and one-half months, without scar formation or pigmentation. A papular rash similar to that present in the gluteal region developed in the anterior deltoid region in August and has remained. Noteworthy is the fact that the patient has complained of nervousness for the last two years and has been subject to spells of crying after overwork.

Repeated Wassermann tests, the Kahn test and many dark field examinations gave negative results. Pus was negative for Coccidioides immitis, blastomycetes and tubercle bacilli. The Frei test was negative. Examination of the stools gave negative results, and that of the urine did not show bromides. Cultures from pus were positive for Staphylococcus aureus.

Material for a biopsy taken from the largest fungating lesion on the left forearm showed features suggestive of a lymphoblastoma; the frequency of mitotic figures in the dense cellular infiltrate was suggestive of a lymphosarcoma. Hesitation was felt in making a diagnosis of lymphoblastoma, however, because of the presence of features of a nonspecific granuloma.

The patient entered the Stanford University Hospitals, where inoculation of rabbits failed to give any information. Roentgenograms of the chest disclosed no abnormalities.

Examination of the blood showed: red cells, 4,870,000; white cells, 11,600; lymphocytes, 25 per cent; monocytes, 4 per cent; platelets, 273,000; reticulocytes, 0.1 per cent; hemoglobin, 97 per cent (Sahli); color index, 1; neutrophils, 68.5 per cent; staff cells, 5.5 per cent; segmented cells, 63 per cent; eosinophils, 1.5 per cent; basophils, 1 per cent.

The smear showed: (1) slight anisocytosis of the red cells; (2) occasional poikilocytosis, and (3) few lymphocytes with slight basophilic cytoplasm but not pathologically young.

Cultures of the blood were negative. A cell count made on August 18 showed no appreciable change.

Roentgenograms of the chest showed normal conditions on September 14, and the study of the blood showed approximately the same values as those found at previous examinations. On September 17 and 18 treatments with filtered roentgen rays were given in two doses of 400 roentgens to the lesion on the left forearm. The lesion has been, so to say, melting since. When the patient was seen four days ago some areas of granulations were still present.

The results of biopsies were as follows: The sections showed secondary inflammatory changes of a granulomatous type. The epidermis showed evidence of prolonged hypertrophy of the rete pegs extending into the cutis; otherwise there were a moderate acanthosis and a well preserved basal cell layer. The epidermal cell layers showed a few mitotic figures in the epidermal cells. There was a lively migration of leukocytes. The cutis showed a dense infiltration of what seemed to be mostly lymphocytes, a few of which had a large nucleus, filling the entire body. Besides, there were numerous lobulated leukocytes; these appeared most frequently at the edge of the ulcer, but were almost absent toward the periphery of the tumor. A few cells resembling foreign body giant cells, possibly only clumped monocytes, were seen. These cells apparently did not conform with the Sternberg or Dorothy Reed cells. The most undisturbed part of the tumor in the periphery of the section showed a uniform lymphocytic infiltrate with few monocytes. Mitotic figures were seen infrequently in this portion of the specimen.

Sections stained for connective and elastic tissue showed almost complete absence of these tissues; only fragments were left. Sections stained with the Becker stain showed complete absence of pigment, both in the basal cell layer and in the cutis. Sections counterstained with indigo carmine and H.8 emphasized the presence of granules stained with prussian blue.

DISCUSSION

DR. A. E. INGELS: This patient has a condition resembling mycosis fungoides. I want to call attention to Dr. Hamilton Montgomery's study of lymphoblastoma which was carried on over a number of years. He has shown that, as Dr. Templeton stated, the condition may start as one form of lymphoblastoma and develop into another, as evidenced by the histopathologic changes.

DR. H. E. MILLER: The cellular infiltration in the sections showed a marked uniformity in the type and size of cells, and to me this suggested lymphosarcoma rather than other types of tumors of the lymphoblastoma group.

LYMPHANGIOMA. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

Miss E. H., aged 18, was seen on Sept. 4, 1923. When the patient was aged 13 months, a tumor the size of a grapefruit was removed from the lateral portion of the right thigh. About five or six years ago the patient noted inflammation of this area after bathing.

She now presents over the right tuber ischii an area 5 by 6 inches (12 by 15 cm.) consisting of reddish tumors from the size of a pinhead to that of a pea; they occur singly or in masses. Some of these are clear, like lymphangiomas. The patient's mother states that the tumors have not grown in recent years. No lesions are visible on other parts of the body. There is slight adenopathy in the right groin. The clinical diagnosis is lymphangioma.

A biopsy made in 1917 by Dr. Ophüls showed lymphangioma.

The patient is presented tonight for suggestions as to therapy. Would it be wise to excise the whole area in order to forestall possible malignant degeneration?

DISCUSSION

DR. HOWARD MORROW: One would have to excise the growth or destroy it by electrocoagulation. Excision would be the best procedure.

DR. H. E. MILLER: My co-workers and I recently had a patient with a deep-seated extensive lymphangioma of one buttock. She was a girl aged 13, who frequently rode a bicycle. The lymphatic spaces were constantly being opened up owing to trauma from the seat of the bicycle, and considerable secondary infection resulted. She was finally hospitalized at a time when no secondary infection was present, and an extensive plastic operation was performed with a good result.

DR. H. J. TEMPLETON, Oakland, Calif.: Has any one any definite idea what proportion of these lesions become malignant?

DR. STUART C. WAY: Lesions of this type often occur, even when they are widely excised. I do not believe that they become truly malignant, unless their recurrence can be so regarded. Complete removal of the entire lesion is more satisfactory than destruction by methods which leave atrophic tissue.

DR. ORLAND F. MONTGOMERY: I feel that excision followed by a plastic operation is the method of choice. I have never heard of malignant degeneration occurring in cases of this type.

LUPUS VULGARIS; EPITHELIOMAS. Presented by DR. H. J. TEMPLETON, Oakland, Calif.

Miss D., aged 50, a native of Scotland, has had lupus vulgaris of the face for forty-two years and has received a great deal of roentgen and radium irradiation in the past.

When I first saw her about nine years ago, the lupus vulgaris involved both cheeks and the nose, which was completely destroyed. Moreover, a great deal of the lupus-bearing areas showed telangiectasia, probably from the irradiation.

During the years I have observed her I have destroyed many involved areas with electrodesiccation. Part of this destruction was undertaken because of lupus vulgaris, but most of it was performed because of multiple epitheliomas, of which I have destroyed thirteen.

About two years ago, when there seemed to be no activity of either the lupus or the epitheliomas around the side of the nose, I referred the patient to Dr. Woolsey for plastic operation.

She is presented tonight to show the satisfactory results he has obtained in rebuilding the nose. In my opinion the plastic operation should be carried on until all the epithelioma-bearing skin is replaced by normal skin.

DISCUSSION

DR. HARRY E. ALDERSON: The results on the face are good so far, but patients with lesions of lupus vulgaris on the face may have lesions in the nasopharynx. I should be afraid that at some time the patient's new nose would become involved.

DR. H. J. TEMPLETON, Oakland, Calif.: I appreciate Dr. Alderson's suggestion. My co-workers and I know full well that the new nose may become tuberculous. One of the reasons, however, for the procedure was to remove the epithelioma-bearing tissue, as I have, in the past years, removed thirteen epitheliomas from the patient's nose.

LICHEN OBTUSUS CORNEUS OR PRURIGO NODULARIS. Presented by DR. C. E. SCHOFF, Sacramento, Calif.

Mr. J. S., aged 23 years, a Filipino, was first seen on June 21, 1934. He complained of a cutaneous eruption which had been present for one month. The first lesion that he noticed was on the inner surface of the right wrist, and his description of it was comparable to that of an insect bite (he attributed the lesion to mosquitoes). Other similar lesions appeared subsequently on the right arm and in the left axilla. Scattered lesions of a similar nature appeared subsequently. These lesions itched intensely and persisted until an infiltrated nodule formed in the skin.

When I saw the patient he stated that he had associated with other members of his race and believed, from the character of the lesions present at that time, that he had scabies. Because of the persistent nodular manifestations it was thought that possibly the disorder belonged to the allergic type of scabies recently called attention to by Scholtz of Los Angeles.

I did not see the patient again until ten days ago. A biopsy was made on one of the lesions, and the patient is presented with the tentative diagnosis of lichen obtusus corneus or prurigo nodularis.

I may say that this is the first time this patient has complained of a dermatosis. The Wassermann and Kahn tests were both negative. The blood count was normal.

DISCUSSION

DR. C. E. SCHOFF, Sacramento, Calif.: This patient was presented with two tentative diagnoses because his condition could not be correlated with anything else. I hesitated about presenting him after the biopsy was made because the biopsy does not show features of lichen planus. As far as prurigo nodularis is concerned, the lesions developed rather late to justify that diagnosis. The sections simply show a chronic inflammatory process. The corium shows only a cellular infiltration about the blood vessels. None of the nodules has resolved, and they have itched considerably. The possibility occurred to me that the patient may have a psychoneurosis, because after the nodule was removed for biopsy the itching was much diminished in all the lesions.

DR. H. J. TEMPLETON, Oakland, Calif.: I thought that this was a case of prurigo nodularis, which term is, I believe, synonymous with lichen obtusus corneus, which, again, is synonymous with Rose Hirschler and Schamberg's multiple tumors of the skin associated with severe itching.

A CASE FOR DIAGNOSIS. Presented by DR. ORLAND F. MONTGOMERY.

For several months this patient, the mother of one child, has had recurring attacks of flaccid vesicles about both ankles. They are exceedingly painful, and she obtains relief only by opening the vesicles. The contents are usually watery, but sometimes they are blood-tinged. At times the feet swell moderately.

There is mottled pigmentation over both ankles. There are many pinhead-sized petechiae, as in Schamberg's disease, and numerous small stellate scars at the sites of former lesions. Four or five vesicles, of the size of a split pea, are present at all times.

In other respects the physical examination gave negative results, save for a questionable Wassermann reaction and the presence of many abscessed teeth. Specimens contained no fungi, and fungicidal treatment caused marked aggravation of the clinical condition.

DISCUSSION

DR. E. D. CHIPMAN: Has fungous infection been ruled out?

DR. ORLAND F. MONTGOMERY: Fungi have been looked for and not found. I do not think that the lesion is mycotic. There is no fever. I considered the possibility of some sort of tuberculous condition. The chest is normal.

DR. HARRY E. ALDERSON: When I examined the lesions I asked Dr. Montgomery whether the patient is receiving compensation. My impression is that the lesions were produced or aggravated by the patient. One must remember that persons can inflict all sorts of lesions on themselves, even down deep into the skin. The peculiar-looking scars impressed me as being of this type. The lesions and the scars have a highly artificial appearance.

DR. ORLAND F. MONTGOMERY: Dr. Alderson's statement is correct. The scars are artificially produced. The patient opens them herself. I have, however, seen lesions before she has opened them.

DR. H. V. ALLINGTON: I think it may be worth while to put an occlusive dressing on the lesions. If the irritation which the patient produces in the lesions could be stopped, one could observe the appearance of the primary condition.

NOTE.—The patient was advised to have all infected teeth removed. The entire upper and lower dentures were removed. Five days after this operation the cutaneous condition had completely subsided, and the skin has since remained normal.

Dr. Howard Morrow, in informal conversation, suggested that this patient's disorder be diagnosed as Bazin's disease of streptococcic type.

LICHEN NITIDUS. Presented by DR. CHARLES ALBERT SHUMATE for DR. HARRY E. ALDERSON.

This Filipino housewife, aged 24, was presented before this society on Feb. 25, 1932 (ARCH. DERMAT. & SYPH. **26**:749 [Oct.] 1932). A record of the case with a photograph of an involved part and a photomicrograph of the biopsy specimen are given in the ARCHIVES. At that time the patient had typical lesions of two years' duration on both sides of the neck and on the right shoulder. There were no subjective symptoms, and the patient was well. No evidence of tuberculosis was discovered. She was given arsenic by mouth; within a month the lesions all disappeared, and the patient stopped taking the medicine.

In August 1934 she returned to the clinic for cutaneous diseases and syphilis of the Stanford University Hospitals with a recurrence of the old eruption. The lesions have been returning gradually for several months. They are typical of lichen nitidus. The family history is unimportant. There is no history of past or present tuberculosis. Roentgenograms of the chest taken this month revealed normal conditions. Complete physical examinations have shown the patient to be in good health. Examinations of the urine and blood, including a Wassermann test, gave negative results.

Recent studies of the tissue taken in 1932 from the left subclavicular region showed no pathologic changes in the epidermis proper except thinning where the underlying nodules of lichen nitidus have pushed the epidermis up. There is no parakeratosis or hyperkeratosis. The rete pegs are elongated and extend into the subpapillary layer. The nodules are built up of round cell infiltration, which consists mainly of lymphocytes interspersed with epithelioid cells and giant cells of the Langerhans type. The rest of the cutis shows no pathologic changes except mild perivascular infiltration. The histopathologic picture is regarded as typical of lichen nitidus.

DISCUSSION

DR. ORLAND F. MONTGOMERY: I am not questioning the diagnosis, but the lesions of lichen nitidus that I have seen were flat-topped and shiny.

DR. HOWARD MORROW: I think that the eruption is typical of lichen nitidus.

TUBERCULID. Presented by DR. N. N. EPSTEIN.

S. G., a girl, aged 13, was first seen in March 1934, when she complained of two similar lesions, one on the extensor surface of the right arm and one on the right buttock. The condition at that time had been present for about one and one-half years, and little change had occurred. There were no symptoms.

There is an annular lesion about 2.5 cm. in diameter on the right arm. In that lesion and in the one on the right buttock the center is clear and there is an active, slightly infiltrated, yellowish-brown narrow border. The border is made up of nodules the size of a pinhead. There are no changes in sensation.

General physical examination gave negative results. Wassermann and Kahn tests of the blood, the Pirquet test and a test with tuberculin ointment were negative. A roentgenogram of the chest showed normal conditions. The blood count and urinalysis gave normal results. Biopsy showed a chronic inflammatory reaction with a number of plasma cells, mainly about the blood vessels.

DR. N. N. EPSTEIN: There is nothing more to add to the preliminary history. While the lesion is suggestive of granuloma annulare, it is not typical of that condition.

DR. H. J. TEMPLETON: My impression from the clinical appearance is that this is granuloma annulare. Was the pathologic picture characteristic of tuberculid?

DR. N. N. EPSTEIN: It was characteristic of a chronic inflammatory process, which is compatible with the diagnosis.

DR. H. V. ALLINGTON: I think that unless there is definite evidence that the patient has tuberculosis I should be inclined to call the condition granuloma annulare rather than tuberculid.

DR. THOMAS J. CLARK, Oakland, Calif.: I should classify the eruption clinically as granuloma annulare. The pathologic picture may bear out that diagnosis or not. In cases of granuloma annulare one cannot always connect up any active tuberculous process with the cutaneous lesions. The lesions occur on the hands or on the elbows. I have seen one patient with lesions on the ears and forehead, and in the majority of cases I have seen there was no reason to suspect that the patient had ever had tuberculosis.

JOHN M. GRAVES, M.D., *Secretary*

Dec. 7, 1934

L. R. TAUSSIG, M.D., *President*

LUPUS ERYTHEMATOSUS RESISTANT TO THERAPY WITH A GOLD, BUT RESPONDING TO TREATMENT WITH A BISMUTH, PREPARATION. Presented by DR. A. E. INGELS.

This patient, a housewife aged 44, was presented in April 1934 because of two semilunar infiltrated, elevated dull red lesions on the right cheek of two years' duration.

Wassermann tests of the blood in March 1933 and July 1934 and examination of the urine gave negative results. The patient is married; she has no children and has had no miscarriages. Her general health has been excellent.

Treatment has consisted of local application of ointments and lotions. Administration of a solution of potassium arsenite and an injection of 0.3 Gm. of neoarsphenamine failed to improve the condition.

On July 17, 1934, a biopsy was made, and after studying the tissue I made a diagnosis of lupus erythematosus disseminatus. The patient then received nine intravenous injections of 5 mg. of gold sodium thiosulphate at weekly intervals.

The lesions did not improve but spread to the left side of the face. The injections of gold sodium thiosulphate were then discontinued, and the patient received eight injections of 2 cc. of bismuth salicylate. Improvement was noted after each injection until at present little of the eruption remains.

The histopathologic report was as follows: Specimens fixed in dilute solution of formaldehyde U. S. P. (1:10) and stained with hematoxylin and eosin and

with the Van Gieson and the Becker stain showed a normal amount of keratosis but no parakeratosis. Plugging of the hair follicles was present in a moderate degree. There was plugging of sweat ducts. The epidermis proper was thinned, showing only three or four layers of cells in places. The basal cell layer showed occasional colliquative degeneration; it was well preserved otherwise except for some intercellular and intracellular edema. The cutis showed a cellular infiltrate consisting mostly of lymphocytes, and a few plasma cells and histiocytes were present. The round cell infiltrate was found perivascularly and around the dermal appendages; it was most pronounced around the hair follicles and less so around the sweat glands. There were no giant cells. The elastic tissue was frayed and split up. The elastica of the vessels was well preserved. In places where the cellular infiltrate was dense there was a tendency toward occlusive changes in the vessels. Formation of collascin and elascin (i. e., degenerative changes of elastic and connective tissue) was well established. Sections prepared with the Becker stain showed absence of pigment over large areas. Other parts showed a normal amount of melanin in the basal cell layer. The diagnosis was lupus erythematosus disseminatus.

DISCUSSION

DR. HARRY E. ALDERSON: When this patient was first seen the opinion was that the lesions were those of a late stage of syphilis. I believe, however, that on the basis of the histologic structure the diagnosis of syphilis can be definitely eliminated. The diagnosis of lupus erythematosus is established histologically; certainly the therapeutic test supported that diagnosis, because the patient had received neoarsphenamine and that drug had no effect on the lesions. The fact that injections of a bismuth preparation were followed by a prompt response does not necessarily indicate that the lesion was due to syphilis; there are many eruptions which respond to treatment with a bismuth preparation, and it is known that such treatment is useful in cases of lupus erythematosus.

There is one interesting matter in connection with the histologic picture in this case, namely, the similarity to Boeck's sarcoid.

I have seen response to treatment with a gold preparation in a case of lupus erythematosus in which two months later there was no response to that type of treatment although therapy with a bismuth compound seemed to be effective.

DR. F. G. NOVY JR., Oakland, Calif.: From the fact that the eruption is involuting it is rather hard to decide clinically whether the disease is lupus erythematosus or not. There is no definite clinical evidence at the present time to substantiate that diagnosis.

DR. H. C. COE, Oakland, Calif: There is a patient now at the health center in Oakland, Calif., who presented definite evidence of lupus erythematosus; the condition has cleared up nicely under treatment with bismuth. In a patient with lupus erythematosus whom I presented some time ago before this society the condition cleared up under bismuth therapy. This patient's lesion, because of its circinate form, suggests an eruption due to syphilis. I think, however, that the whole diagnosis depends on the histologic picture, and the slides have not been presented.

DR. L. R. TAUSSIG: My co-workers and I have treated a number of patients with lupus erythematosus with bismuth, and, on the whole, the results have been disappointing.

A description of the histologic changes is not as satisfactory as an examination of the sections, but in this instance the description did not suggest lupus erythematosus. I was inclined to believe that the patient had syphilis. I believe that a single dose of neoarsphenamine is not an adequate therapeutic test. However, the histologic picture, as described, fits better with that of sarcoid, and I am inclined to think that the condition is sarcoid rather than syphilis or lupus erythematosus.

DR. C. J. LUNSFORD, Oakland, Calif.: I do not see how any one can differentiate between lupus erythematosus and syphilis from the patient's appearance tonight. I

have seen cases of lupus erythematosus that have responded to treatment with bismuth and not to that with a gold preparation.

DR. ERNEST K. STRATTON: I have never seen a case of lupus erythematosus of such long standing without the presence of some atrophy, and I did not see any atrophy in this case. I am inclined to believe, with Dr. Taussig, that this is not a case of lupus erythematosus but one of syphilis or sarcoid.

DR. ORLAND F. MONTGOMERY: When bismuth is used in the treatment of lupus erythematosus, what preparation is used?

DR. H. C. COE, Oakland, Calif.: The patient who is being treated in Oakland, Calif, receives bismuth salicylate.

DR. HARRY E. ALDERSON: This patient had two Wassermann tests; she has been examined carefully, and there is no evidence, from the clinical or serologic data or from the past history, that would support a diagnosis of syphilis. There is atrophy. Possibly it is more apparent in the daylight. The lesions do not conform to the discoid type of lupus erythematosus, but they are characteristic of forms bordering on sarcoid.

Little significance should be attached to the negative result following the injection of 0.3 Gm. of neoarsphenamine, but the rather prompt response to treatment with bismuth salicylate appears to be important and should be interpreted as an indication of lupus erythematosus.

CHRONIC ARSENICAL KERATOSES AND PIGMENTATION: BOWEN'S DISEASE. Presented by DR. HARRY E. ALDERSON.

J. S., a Polish Jew aged 50, presents several hyperkeratotic lesions on the trunk, nose, left ear and palms. On the abdomen there is a superficial ulcer 3 cm. in diameter, the surface of which is covered with a film of pus. On the right side of the neck there is an irregular plaque with raised borders which is somewhat nodular but not translucent. There are dull red plaques of psoriasis scattered over the body.

I first saw the patient in 1913. At that time he presented a deeply pigmented skin and hyperkeratosis of the palms and soles. There were also keratotic areas on the edges of the eyelids and on the ears and nose. The patient has taken arsenic in the form of pills for psoriasis since 1907. For several years he has taken as many as 15 pills a day. They contained from 0.0001 to 0.0004 Gm. of arsenous acid. Since 1914 he has not taken arsenic in any form.

At that time general physical, including neurologic, examination gave essentially negative results. The patient reported at irregular intervals at my office until 1918, at which time the pigmentation and many of the keratoses had for the most part disappeared.

He was seen in 1925. The cutaneous condition was fairly good. The patient had a genito-urinary infection at that time. In 1929 he was treated for arthritis at the outpatient department of the Stanford University Hospitals. Psoriasis had returned. The Wassermann test was negative. Examination in 1925 in the outpatient department revealed possible malignant degeneration at the site of an old lesion on the right side of the abdomen and on the palmar surface of the fourth finger. The lesions were removed surgically.

Reports on histologic examinations (July 26, 1932, and Dec. 3, 1934) were as follows: Sections previously taken at the Stanford University Hospitals were examined at the surgical pathologic laboratory, and a diagnosis of Bowen's disease, contra-indexed as epithelioma, was made. A study of some of the sections showed obvious epitheliomatous changes with profound disarrangement of the basal cell layer as well as of the prickle-cell layer. Mitotic figures were numerous. There was a great variety in the size of the cells, some of which were giant epithelial cells. There was a tendency to whorl formation and suggestive perforation, although the latter was not obvious. In other parts of these sections there were only comparatively mild disturbances and the basal cell layer seemed well preserved,

although mitotic figures occurred frequently in those parts also. This last condition seemed to be of the type that Bowen described.

Another biopsy, made on Dec. 3, 1934, showed approximately the same condition but lacked the changes characteristic of Bowen's disease. The degeneration characteristic of squamous cell epithelioma seemed obvious, as indicated heretofore. The diagnosis was squamous cell epithelioma; in parts of the section, Bowen's disease only.

The severe inflammatory changes in the cutis with occlusive changes in the vessels and almost complete obliteration of the dermal characteristics were noteworthy.

DISCUSSION

Dr. Harry E. Alderson: This patient took enormous doses of arsenic for a number of years, and that held his psoriasis in abeyance. A marked pigmentation developed but subsided. He has not taken arsenic since 1917. During the exacerbation of the eruption he had an epithelioma on the nose. Dr. Graves and Dr. Coe, I think, saw him when they were students. As he has taken no arsenic since 1917 and it is believed that he has not absorbed any since that time, the fact that the cornlike lesions in the palms persist, is interesting. He has a lesion on the ankle that resembles Bowen's dyskeratosis. The lesion on the neck is definitely a squamous cell epithelioma.

It is interesting to speculate how the arsenic has been retained all this time and what has been the mechanism of the formation of epitheliomas and of the lesions that look like Bowen's disease.

Dr. N. N. Epstein: I agree with the diagnosis of arsenical hyperkeratosis and pigmentation.

Dr. H. J. Templeton, Oakland, Calif.: One must remember that psoriasis sometimes ends in epithelioma. Carroll Wright reviewed cases in which psoriasis developed into squamous cell epithelioma, and he suspected that arsenic was an etiologic factor in all the cases.

Dr. Ernest K. Stratton: How much value would tests of the urine for arsenic have now, so long after injections of arsenic have been given? Would not a study of the skin for arsenic be more important than studies of the urine?

Dr. C. E. Schoff, Sacramento, Calif.: I do not think that the arsenical aspect of this case is as interesting as the question of the diagnosis of Bowen's disease. Bowen's disease has always been a controversial subject, and a diagnosis of Bowen's disease is always a matter of difference of opinion. I think that the interesting point is whether the patient has Bowen's disease. I should like to hear this discussed.

Dr. H. V. Allington: If I remember correctly, Dr. Satenstein has slides showing that when arsenical keratoses degenerate they sometimes produce squamous cell, and sometimes basal cell, epitheliomas; sometimes the changes of Bowen's disease appear. In the same section one can sometimes find all three types of degeneration.

Dr. L. R. Taussig: The phenomenon of dyskeratosis is a rather common one, and the histologic changes that occur in that condition are seen in various disorders. Dyskeratosis is only a part of what is called Bowen's disease, and dyskeratosis alone should not be given too prominent a place in a description of the disease.

It seems to me that an overconservation of arsenic results in cutaneous changes which are, in many ways, analogous to the changes that occur after exposure to roentgen rays and that the presence of arsenic in the skin or urine is entirely beside the point. After degeneration has set in the lesions are apt to progress whether ingestion of arsenic is continued or not. This is true also of changes following exposure to roentgen rays. One sees keratoses from irradiation that are benign, and later epithelioma may develop. I think that exactly the same thing can occur in arsenical dermatosis.

DR. H. V. ALLINGTON: Dr. Satenstein has, I believe, also demonstrated metastases from cutaneous lesion to distant glands and distant organs. The histologic picture that occurs in the original growth can occur in the metastases, and this, I think, indicates that the disease is a definite type of cancerosis.

PSEUDO-ATROPHODERMA COLLI (IDIOPATHIC ATROPHY). Presented by DR. C. J. LUNSFORD, Oakland, Calif.

Miss L. M., aged 22, says that when she was 17 years old she first noted brownish, dry, scaly areas on the skin of the neck.

For six months before the first appearance of the lesions she had been sickly and had attended school only every other day because of weakness and fatigue. In the summer she acquired a sunburn, and after the desquamation she noticed the thin depigmented areas.

Occasionally the areas itch after contact with woolen clothing or after bathing. Otherwise there are no symptoms.

The patient has lived in Washington and in California all her life. The development and menstrual history are normal.

General examination gave normal results. The basal metabolic rate was —15 per cent. The patient is now taking thyroid extract daily.

There is a dry, scaly, inelastic, atrophic, wrinkled, more or less translucent eruption on the upper portion of the chest and on the neck, particularly in front. A few similar lesions are present on the lower part of the loin and similar white, atrophic, oval, pea-sized, scaly lesions are scattered on the flexor surface of the arms. There is no hardness or induration. The skin of the anterior portion of the chest when lifted appears light and lacking in elasticity. The axillae show pigmented scaling. The backs of the hands show spots of depigmentation intermingled with areas of hyperpigmentation.

On Dec. 6, 1934, a superimposed dermatitis appeared; it was due to ammoniated mercury or chlorine in water in which the patient had been swimming.

Examination and culture of scales for fungi gave negative results three times.

DISCUSSION

DR. C. E. SCHOFF, Sacramento, Calif.: I do not think that the eruption has the clinical appearance of idiopathic macular atrophy. I have seen one case of that disorder and the eruption was generally distributed over the body and not confined to any particular area. It had existed for several years. There may be atrophy in these lesions, clinically. I should like to see a biopsy specimen to ascertain whether atrophy is present.

DR. ORLAND F. MONTGOMERY: I treated a patient with a somewhat similar disorder. There was no atrophy. The superficial appearance of the lesions was the same as in this patient. Under therapy, improvement occurred and lasted for about three months; then there was a recurrence. Probably this patient's condition is not of the same type if there is atrophy.

DR. N. N. EPSTEIN: In individual cases of idiopathic macular atrophy which I have seen and in cases of macular atrophy following syphilitic infection, there was no change in the superficial portion of the epidermis. In this case I am not certain that there is a definite atrophy, and the superficial scaling leads me to think that clinically the disorder is not an idiopathic macular atrophy.

DR. ERNEST K. STRATTON: I think that there is definite atrophy in those lesions, and I should classify the condition as an atrophy probably of endocrine origin.

DR. H. J. TEMPLETON, Oakland, Calif.: Because of the presence of atrophy and because of the distribution, which is largely on the neck, I should class this case as one of pseudo-atrophoderma colli such as that described by Becker and Muir (Becker, S. W., and Muir, K. B.: Pseudo-Atrophoderma, ARCH. DERMAT. & SYPH. **29**:53 [Jan.] 1934). An attempt will be made to obtain a biopsy specimen and to stain the sections in order to substantiate this diagnosis.

Four years ago Dr. Morrow and I saw in Doctor Oppenheim's clinic a patient in a grave condition with one type of atrophy. Several years later I saw that patient, and she had recovered. She had received injections of one of the ovarian hormones.

The early pathologic change seen in macular atrophy is a perivascular round cell infiltration with no atrophy. I should think that in the early erythematous stage only the condition would be favorably influenced by roentgen therapy.

DR. C. J. LUNSFORD, Oakland, Calif: Dr. Ingels suggested the possibility of the eruption's being an atrophic type of lichen planus.

A CASE FOR DIAGNOSIS. Presented by DR. FRANCIS TORREY.

Miss I. G., aged 21, was first seen on Oct. 5, 1934, because of a pustular eruption on the forehead and back.

This eruption became more extensive within the next two weeks, involving the entire trunk and extending along the extremities and onto the hands. At that time there were no lesions on the mucous membranes.

A month later some of the pustules on the body had involuted, and new ones had appeared, and at that time several small superficial, somewhat painful ulcers had appeared on the vulva and on the mucous membrane of the lower lip.

The patient and her 6 month old child had gonorrhea. The patient is being treated, and smears are now negative for gonococci. There is no history of ingestion of drugs. Physical examination and laboratory studies, including a Wassermann test, gave negative results.

Smears and cultures from the pustules show only staphylococci. Smears from the vaginal ulcers are negative for Bacillus crassus but show some acid-fast material, probably smegma. The report from the inoculation of guinea-pigs has not been received. No organisms were seen in a section of tissue from a pustule stained with Gram's stain and with an acid-fast stain.

Histologic examination showed a typical but moderate inflammatory reaction with perivascular infiltration of polymorphonuclear leukocytes and a few lymphocytes in the corium.

After one injection of neoarsphenamine, ten days ago, no change has occurred in the lesions.

DISCUSSION

DR. F. G. NOVY JR., Oakland, Calif.: I believe that the eruption either is due to a drug or is a toxic manifestation. Certainly the results of the biopsy do not indicate that it could be a tuberculid. When patients are asked concerning ingestion of drugs they sometimes answer negatively even though they are taking some drug. I think that the patient is taking iodides.

DR. MERLIN MAYNARD, San Jose, Calif.: Is the patient receiving douches of any sort?

DR. FRANCIS TORREY: That has been checked, and she is not. I think that merthiolate was applied when the patient was in the hospital.

DR. MERLIN MAYNARD, San Jose, Calif.: My impression is that the eruption is due to iodide or to a bacteremia, perhaps to a gonococcic bacteremia.

DR. HARRY E. ALDERSON: Dr. Maynard's suggestion that the condition may be a metastasis from a gonococcic infection is interesting. I have seen several such cases, but they were always associated with arthritis. I think that several conditions may be present. The patient has acne vulgaris on the face, and acne is sometimes an expression of systemic tuberculosis.

DR. C. J. LUNSFORD, Oakland, Calif.: Has any one ever seen an eruption due to a bromide or iodine involving the mucous membrane? And is there any drug other than bromides or iodides that will produce a lesion followed by such scarring?

DR. H. V. ALLINGTON: I wonder what the histologic picture showed. I was under the impression that to make a diagnosis of papulonecrotic tuberculid it was unnecessary to find a tuberculoid structure.

DR. ERNEST K. STRATTON: The disease may be parapsoriasis varioliformis. I presented a patient with a similar condition a few years ago for diagnosis, but the disease was not recognized until several months later.

DR. H. J. TEMPLETON, Oakland, Calif.: Has a Weil-Bilotti test of the urine been made or has hypertonic saline solution been given?

DR. FRANCIS TORREY: No.

DR. H. J. TEMPLETON, Oakland, Calif.: Like Dr. Maynard, I advise further search for evidence of a gonococcic infection. Moreover, I suggest that an intradermal test be made with a suspension or extract of a known strain of B. crassus as an antigen.

DR. FRANCIS TORREY: The patient has had no chills and no fever. She has been perfectly able to go about and has complained only of a feeling of lowered vitality. A test for B. crassus will be made. Repeated smears and cultures have not shown the presence of B. crassus.

ADENOMA SEBACEUM. Presented by DR. H. V. ALLINGTON.

M. H., aged 18, presents numerous lesions, varying in diameter from 1 to 4 or 5 mm., distributed symmetrically over the nose and the central flush areas of the cheeks. The lesions are raised and firm and show slightly irregular surfaces, and both the lesions and the normal skin between and about them show small, irregular areas of telangiectasia. In addition the patient presents scattered tiny digitate and pedunculated fibromatous tags on the gingivae.

Cutaneous lesions were first noted seven or eight years ago, and they have not changed appreciably in the past year or two. The patient is in good general health and is doing her work adequately as a freshman at the university.

She has one brother, aged 5, who is well. Neither he nor any member of the family, as far as the patient is aware, has ever had a similar disorder.

DISCUSSION

DR. H. J. TEMPLETON, Oakland, Calif.: There are two types of adenoma sebaceum. One is not an adenoma of the sebaceous glands at all but belongs rather to the fibroma group. It is said by some authors to be closely related to Recklinghausen's disease.

In regard to adenoma sebaceum (Pringle's disease) Highman made the statement that in any group of from ten to fifteen dermatologists probably only one had seen a case of true adenoma of the sebaceous glands. I believe that this case is one of adenoma sebaceum related to the fibroma of the Recklinghausen group.

DR. J. M. GRAVES: In regard to treatment it was suggested that these lesions be desiccated. I did not know that desiccation is preferable to electrolysis.

DR. MERLIN MAYNARD, San Jose, Calif.: I think that there is one point in favor of desiccation: When a desiccation needle is put in the lesion a large number of blood vessels at the point of entry are coagulated. For this reason, desiccation is much better than electrolysis. One does not need simply to burn down the lesions. It is more the destruction of vascular tissue that is desired, and desiccation accomplishes that more satisfactorily.

DR. H. V. ALLINGTON: I believe that one can get the same blanching of telangiectatic vessels by electrolysis.

DR. L. R. TAUSSIG: In the use of destructive methods of therapy the most important thing is that the operator be familiar with the method he is handling. In the office my co-workers and I have used electrolysis infrequently. We have used electrocautery and desiccation more often. I am quite sure that when properly used electrolysis is as effective in destroying small areas as the other two methods.

I believe that this patient has a typical Pringle type of adenoma sebaceum, and my opinion is based on the literature of the fibromatous variations of Recklinghausen's disease. This is the first opportunity that I have had of seeing any of these fibrous lesions associated with adenoma sebaceum.

Dr. C. E. Schoff, Sacramento, Calif.: Does not the Pringle type of adenoma disappear without treatment? This patient is only 18 years old. Is the condition getting progressively worse?

Dr. H. V. Allington: The lesions have not changed noticeably in the past year or two.

Xanthoma Tuberosum Multiplex. Presented by Dr. H. V. Allington.

Mr. R. G., aged about 35, when seen on Sept. 18, 1934, presented raised, firm, pale lemon-yellow, infiltrated papules over the extensor surfaces of the elbows and over the buttocks and lateral surfaces of the thighs; there were a few lesions over the extensor surfaces of the knees and about the lower portion of the trunk. Similar infiltrations were present in the folds of the flexor surfaces of the fingers and palms. The lesions were first noted about a month previously and were associated with some itching and some soreness in the joints of the fingers and hands.

The urine contained a trace of albumin; a biopsy was made, and the specimen is available for examination. No opportunity was given for further laboratory studies. The patient is presented with a diagnosis of xanthoma tuberosum multiplex.

DISCUSSION

Dr. H. V. Allington: I should appreciate suggestions for treatment. The patient is on diet with a low carbohydrate content.

Dr. J. L. Fanning, Sacramento, Calif.: My co-workers and I had a patient whom Dr. Faber saw who had a cholesterol content of 1,500 mg. per hundred cubic centimeters of blood. Dr. Faber prescribed a diet with a low cholesterol content, and much improvement resulted.

Dr. J. M. Graves: May I ask about the degree of improvement to be expected in diabetic xanthoma?

Dr. H. J. Templeton, Oakland, Calif.: Xanthoma diabeticorum can occasionally be completely cleared by controlling the diabetes.

Dr. Merlin Maynard, San Jose, Calif.: I had a patient, a child 7 months old, with active xanthoma multiplex. I looked up the literature published since 1932. In cases of diabetes improvement may occur, but in cases of xanthoma multiplex improvement is more rare.

Dr. N. N. Epstein: All patients with that disease do not have a hypercholesteremia.

Dr. O. P. Diederich, Fresno, Calif.: I wonder what effect di-nitrophenol would have in a case as extensive as this is. The patient is greatly overweight.

LOS ANGELES DERMATOLOGICAL SOCIETY

Nelson Paul Anderson, M.D., *Secretary*

Regular Monthly Meeting, Jan. 8, 1935

Moses Scholtz, M.D., *in the Chair*

Lichen Planus and Lichen Spinulosus Following Antisyphilitic Treatment. Presented by Dr. Irving R. Bancroft.

Mr. L., aged 26 years, single, had a syphilitic chancre four months ago. No secondary eruption occurred. Treatment has consisted of eight injections of neoarsphenamine and nine injections of a bismuth preparation. The present eruption began three months ago. At first there were red, macular, oval lesions which in places were deeply pigmented and have remained so. At the same time the follicles

became hypertrophied, and in places the top of the follicle is covered with a short keratinlike point which, when the hand is rubbed over the skin, produces a feeling like that of a file. This patient is presented because of the sharp keratin-like projections which are often seen in cases of arsenical toxemia.

DISCUSSION

DR. KENDAL FROST: I am inclined to think that if any characteristic change occurs in the skin as a result of arsenic medication that change is perifollicular. In the cases of acute generalized erythroderma due to arsphenamine the first change appears as a small pink, oval macule in which the follicles are prominent. In this case the eruption with its pigmentation and horny follicular projections could correspond to the acute early phase, from which it differs only in being chronic.

DR. MOSES SCHOLTZ: This condition is more uncommon than any I have seen before. The lesions are lichenoid and due to arsenic medication. It is my impression that the distribution of these spinulous lesions is entirely too generalized. The lesions cover the whole body, while all the spinulous lesions I have seen were grouped. I have never before seen patients in whom the spinulous lesions covered the whole body. In spite of the patient's statement to the contrary, I think that the condition may be congenital. I should like to see the patient later, for lichen planus clears up, and I think that the spinulous lesions will persist indefinitely.

DR. W. H. GOECKERMAN: I think that Dr. Bancroft's observation is correct. I agree with the assumption that both the hyperkeratotic papules and the spinulous lesions are due to arsenic. As one looks at the lesions, especially at the pigmented ones, the first thought is that the patient has a truly lichenoid eruption. However, when the pigmentation is examined with some care it is seen to involve the hyperkeratotic papules as well as the other parts of the skin, and I think that this agrees fairly well with what has been seen before. That these pigmentations are as common as they are in Dr. Bancroft's experience is somewhat surprising. I remember having seen two or three similar eruptions due to medication. It is possible that the predominance of the condition in certain races or the type of drug employed may explain his experience. This patient's appearance tonight prompts me to agree with Dr. Bancroft's conception.

DR. H. S. CAMPBELL: The whole discussion in this case seems to be a little ambiguous. May I ask whether the patient is presented as having an arsenical eruption or lichen planus and lichen spinulosus?

DR. IRVING R. BANCROFT: He is presented as having lichen planus and lichen spinulosus.

DR. C. R. HALLORAN: These conditions are lichenoid eruptions produced by arsenical medication. French authors have written extensively on this subject. Histologically the picture is that of lichen planus together with this brown pigmentation. This patient also presents lichen spinulosus. Dr. Bancroft and I have one patient under observation at present who has typical lesions of lichen planus in the mouth.

DR. NELSON PAUL ANDERSON: I think that Dr. Bancroft is to be commended for presenting patients with this condition at meetings of the society, and I hope he will not allow our discussions to prevent his presenting others with similar diseases. I think he has made a real contribution to the study of lesions produced by arsenical treatment. I wonder whether any of the patients he has presented here have received further treatment with arsenic and whether or not patch tests have been made.

DR. SAMUEL AYRES JR.: I feel that the follicular hyperkeratosis is due to arsenic and the lichenoid lesions are partly due to the same cause, but I cannot help but believe that syphilis plays some part in the production of these lesions. The chancre occurred only four months ago. I believe that if this arsenical reaction had not occurred so shortly after the primary manifestation of syphilis the lesions would look different. This eruption may be regarded as a secondary syphilid

complicating an eruption due to arsenic. In regard to the lesions of lichen planus and the lesions under consideration, the two kinds may be alike histologically, but I do not think that they are the same from a clinical point of view. These arsenical lichenoid eruptions frequently occur on the face and seldom on the penis, which is the reverse of the usual distribution of true lichen planus.

Dr. Irving R. Bancroft: In answer to Dr. Anderson's question, I wish to state that I have not given any more arsenic to the patients to whom he referred. In one case the pigmented lesions lasted two years after the arsenic medication was discontinued. I have not made the patch test. I have a patient with a similar eruption who did not receive bismuth. Originally I thought that an eruption of this type was a rash due to bismuth.

Dr. H. S. Campbell: I agree with Dr. Ayres. I believe that the eruption is a combination of arsenical dermatitis and a secondary rash of syphilis and that the manifestations of secondary syphilis are due to the therapy. Usually in cases of lichen planus and of lichen spinulosus the lesions are grouped, and while clinically these spinulous and keratotic lesions may simulate each other, lesions of lichen planus and lichen spinulosus are rarely found so evenly distributed over the entire body.

Dr. George F. Koetter: At present I have a man under observation who presents a picture identical with that shown by Dr. Bancroft's patient. After an exfoliative dermatitis due to neoarsphenamine given elsewhere there developed lichen planus with lesions fairly well generalized. As some bismuth preparations contain arsenic, I am giving the patient weekly intramuscular injections of corrosive mercuric chloride, 1/8 grain (0.008 Gm.) to 1 cc., with excellent results. I believe that the lesions are a recurrent secondary syphilid rather than true lichen planus.

Dr. Stanley Chambers: I have always been of the opinion that lesions of this type were recurrent syphilids. I agree with Dr. Ayres and his point of view.

Trophic Ulcer. Presented by Dr. Moses Scholtz.

G. Z., a man, has an irrelevant family history and has always been in good health. The present illness started after he sustained an accidental injury to the foot while crushing stones three years ago, with subsequent deep infection. The large toe was amputated. He presents an ulcer of two years' duration, which heals over when the patient remains in bed and recurs when he is up and about. His general appearance is that of a healthy man. Examination by two neurologists revealed sciatica, atrophy of the muscles and anesthesia of the lower half of the leg. The Wassermann reaction was negative. No treatment has been administered recently.

DISCUSSION

Dr. Stanley Chambers: I suggest the diagnosis of linear scleroderma caused by injury.

Dr. Samuel Ayres Jr.: I saw a patient with a condition somewhat like this in the hospital a year ago. He had had an injury to the foot, and subsequently disturbances of a trophic nature continued to develop in the leg. While there is an inclination to regard such lesions as factitious, some trophic element may have been overlooked. I think that cases of this type deserve a good deal of study. I agree with Dr. Chambers' remarks that the ulcer is a sclerodermatous change with lesions of a trophic nature.

Dr. Moses Scholtz: The suggestion of Dr. Chambers is interesting, but a sclerodermic ulcer would hardly heal up spontaneously when the patient remains in bed. There was osteomyelitis also, and a few operations were performed to remove fragments of bone.

Dr. H. C. L. Lindsay: In these cases of trophic ulcer one can usually detect some disturbances higher up in the nerves. It is usual for the condition to extend downward. When an injury affects the central nervous system disturbances are

likely to occur in that system. When a neuritis lasts over a year there is nearly always some atrophy in the muscles supplied by the affected nerve; on the other hand, neuralgia may not cause atrophy.

DR. CHARLES R. CASKEY: This patient exhibits a loss of sensation several inches from the ulcer. The ulceration is evidently due to circulatory as well as to neural disturbances.

DR. H. S. CAMPBELL: I was able to elicit evidence of anesthesia around the scar and could not note atrophy of any adjoining muscles. To me the lesion appears to be a linear scar with a keloidal tendency, and it is suggestive that, according to the history, the lesion when it breaks down does so in its upper third. The patient also states that before the ulcer breaks down the foot and ankle always swell and that this occurs when he uses the foot for twenty-four hours. If the breakdown were due to deficient aeration because of this edema, the ulceration would normally occur in the lower third of the scar line. Furthermore, if the ulcer were a trophic one it would not have the fairly healthy appearance at the border which it presents. And certainly the history of its spontaneous healing within about twenty-four hours after the patient returns to bed and the foot is elevated, which Dr. Scholtz commented on, absolutely rules out any possibility of trophic ulceration, for tropic ulcers are universally recognized as being notoriously indolent.

PSORIASIS ACCOMPANIED BY SCARS AS A RESULT OF TREATMENT BY A CAUSTIC ACID. Presented by DR. H. C. L. LINDSAY.

L. G., a school girl aged 19, is an Armenian. A dry, scaling, patchy cutaneous disease, involving mostly areas on the scalp and lower parts of the legs, began about five years ago. The lesions are the size of a half-dollar and have friable, silvery white scales. There are scars in the scalp and on the legs which, the patient alleges, remain from some treatment. New lesions appear in the old scars. Some of the lesions have disappeared without leaving any trace. No new lesions have appeared on the knees or elbows. The rash is essentially psoriasiform. The Wassermann reaction was negative.

DISCUSSION

DR. H. C. L. LINDSAY: I was intrigued by this eruption when I first saw it. I thought at first that these scars were due to the disease, but I believe that the patient had psoriasis and was treated by an Armenian doctor who probably used nitric acid to remove the lesions. She had definite scars on the scalp: Lesions of psoriasis have appeared in the scars. This girl was in Armenia during the massacres, and there is a possibility of her having syphilis, although the Wassermann reaction of the blood has been negative. No test of the spinal fluid has been made. The report on the biopsy is not available.

DR. H. S. CAMPBELL: I should call the condition an atrophic type of psoriasis.

DR. C. R. HALLORAN: This patient was on Dr. Frost's and my service at the Los Angeles County Hospital two months ago, and there was a definite history of acid having been applied to all the sites at which the scars are now seen. I think that the condition is purely an effect of treatment to psoriatic lesions.

DR. STANLEY CHAMBERS: Regardless of the history, the archiformation, induration and pigmentation lead me to suspect a psoriasiform syphilid.

DR. H. C. L. LINDSAY: There are no lesions on the knees or elbows.

DR. H. S. CAMPBELL: Please do not understand that I am referring to the many scars which are present as being part of what I term an atrophic type of psoriasis. To my mind the scars have no part whatever in this picture, as they are patently of artificial character. I am referring to the essential lesions which are present and which are not due to previous forms of treatment. They have been present for many years, and in my opinion, they are simply due to psoriasis of atrophic character.

DR. MOSES SCHOLTZ: I never heard about atrophic psoriasis. I wish Dr. Campbell would refer me to literature from which I can obtain information about that disease.

DR. H. S. CAMPBELL: I do not believe that one could find the term atrophy, as applied to psoriasis in the present instance, in the literature. Even the Continentals, who possess a wider descriptive terminology than the English-speaking peoples, failed to utilize two terms in describing psoriasis which might just as fairly have been included, viz., hypertrophic and atrophic. I came to recognize the justification for these two descriptions during the period I was scraping scales for a new therapeutic procedure. These scales in different cases ranged from a thickness that clinically, in one case at least, had been diagnosed as a diffuse keratoderma blenorrhagicum, to a thinness that made it practically impossible to obtain a single scale without breaking through the pellicle to draw blood. While histopathologically the lesions manifest hyperkeratosis, I still maintain that their clinical differences warrant the utilization of the terms.

DR. STANLEY CHAMBERS: Staining of material obtained for a biopsy on one of the active lesions with Krajian's stain (a modification of Dieterle's method for demonstrating Spirochaeta pallida) and a provocative Wassermann test of the blood would help to clarify the situation.

DR. H. C. L. LINDSAY: I looked over some of the literature and noted that Crocker mentioned the occurrence of scars after psoriasis; he said that in some cases there have even been keloids.

EPITHELIOMA (BASAL CELL, ATROPHIC, ARSENICAL); ARSENICAL KERATOSES. Presented by DR. SAMUEL AYRES JR.

S. V. H., a Canadian woman aged 59, presents lesions on the face, neck and scalp. The eruption began twelve years ago with one lesion on the right side of the face and one on the forehead; at first the lesion on the face was the size of a dime. It gradually increased until now it is the size of a hand. The lesion on the forehead cleared spontaneously and recurred one year ago. The lesions on the neck have been present for four or five years, and those on the scalp, for two or three months. No subjective sensations are present. The lesion on the scalp is slightly sensitive. The patient had a chronic discharging sore on the right side of the neck; this was destroyed by cautery one year ago and has not recurred. At the age of 10 years the patient had a scattered eruption of red plaques with white scaling which appeared on the scalp, elbows, knees and trunk. No lesions of this type have been present for the past four or five years. She had taken a solution of potassium arsenite at intervals over a long period. The eruption clears under this medication but recurs. On the right side of the face is a large, sharply defined area, about the size of the palm of an adult exclusive of the fingers, extending from the ear to the jaw, cheek and neck. This area presents a sharply defined white vitiligo-like center with a few scattered freckle-like macules and a sharply defined threadlike pearly border. There are also brownish-red threadlike scaly lesions on the back of the neck and on the forehead and left ear. The palms and soles show numerous punctate keratoses. In the scalp are three or four brownish-pink, slightly scaly macules without a typical pearly border.

DISCUSSION

DR. H. C. L. LINDSAY: The lesions on this patient's face, especially the lesion on the forehead, remind me much of the lesions of Bowen's disease.

DR. W. H. GOECKERMAN: I am of the opinion that the lesion is a superficial cicatrizing epithelioma.

DR. STANLEY CHAMBERS: I should classify the condition as a cicatrizing epithelioma.

DR. SAMUEL AYRES JR: I saw this patient for the first time this morning, and I think that it is the most striking example of the condition I have ever seen. The lesion on the face looks like vitiligo.

MANHATTAN DERMATOLOGIC SOCIETY

ISADORE ROSEN, M.D., *Chairman*

MIHRAN B. PAROUNAGIAN, M.D., *Secretary*

Jan. 8, 1935

PSORIASIS PALMARIS ET PLANTARIS. Presented by DR. MIHRAN B. PAROUNAGIAN.

Mr. K., aged 75, presented himself at the dermatologic clinic of the Bellevue Hospital for the treatment of lesions on the hands and feet. Palmar lesions had begun about four months before, and later an eruption appeared on the feet. No lesions had been noticed on the body, and the patient did not mention having had the trouble before.

On the palms there are patches of hyperkeratosis with scaling and fissures. Similar patches are present on the fingers, extending to the nails. The fingernails are distorted and discolored. On the soles, extending slightly over the dorsa of the feet, there is similar extensive hyperkeratosis in larger and smaller patches, but there the bases of the lesions have a definite coppery erythema. The lesions on the feet, too, are scaling and fissured and involve all the toes, extending in many cases to the nails. The toe-nails are markedly irregular and distorted.

There is an isolated erythematosquamous patch on the right external malleolus, and a few smaller patches are present on the left leg. On the dorsal side of the penile sulcus, there is a thickened, scaly area. No other lesions are visible on the body, and the scalp is clean. The Wassermann reaction was negative.

DISCUSSION

DR. FRED WISE: I accept the diagnosis as presented. However, I think it is necessary to obtain a microscopic examination in order to make a positive diagnosis. In many cases in which there is no other evidence of psoriasis the possibility of palmar and plantar keratoderma must be considered.

DR. GEORGE C. ANDREWS: The absence of psoriasis of other parts of the body and the short duration of the eruption on the soles and palms point to the diagnosis of arsenical keratoderma. The appearance of the eruption on the palms and soles is more suggestive of this condition than of psoriasis. I suggest that the arsenic content of the blood be investigated.

LICHEN PLANUS AND LICHEN PLANUS NODULARIS OF THE LOWER EXTREMITIES. Presented by DR. ISADORE ROSEN.

L. C., a boy aged 8, born in the United States, was brought to the clinic for cutaneous diseases of the Mount Sinai Hospital for a condition which began about three months ago, first appearing on the left leg and later spreading to the right leg. In the past three weeks the eruption has involved the entire trunk and upper extremities. The patient states that the eruption is only moderately itchy. No other member of the family has any type of cutaneous disease.

The lesions are scattered extensively over the entire body, with the exception of the face and the palms and soles. They vary in size from that of a pinhead to that of a dime. There are large coalescent lesions on the forearms and legs.

The individual lesions are of two types: flat polyhedral, smooth, shiny violaceous papules and irregular papules larger and more erythematous than those of the first type and usually covered with an adherent scale. There are no lesions in the mouth or on the penis. On the scalp are numerous patches of whitish scales, which are circumscribed, little raised and seem to have little, if any, inflammatory component. There are well marked examples of Koebner's phenomenon on the arms and legs. The microscopic examination of the scalp for fungi gave negative results.

DISCUSSION

DR. MAX SCHEER: The lesions on the extremities are typical of lichen planus. Those on the scalp look like lesions of psoriasis. One cannot make a diagnosis of lichen planus for those lesions without a biopsy.

DR. LUDWIG OULMANN: I regard the condition lichen planus and lichen planus hypertrophicus. The case needs to be investigated more thoroughly.

DR. E. WILLIAM ABRAMOWITZ: The lesions on the scalp may be considered as lichen planus if they appeared at the same time as the lesions on other parts of the body. The latter are typical of lichen planus. A biopsy of a lesion on the scalp would add confirmatory evidence for the diagnosis of lichen planus of the scalp.

DR. J. FRANK FRASER: The lesions on the body are typical of lichen planus. I agree with the presenter's views that the patient has only lichen planus.

DR. MIHRAN B. PAROUNAGIAN: I think it reasonable to presume that all the lesions are caused by lichen planus. The focus of infection interests me. One patient whom I treated for several years finally had the teeth examined with roentgen rays, and several infected roots were found. When these foci were removed the patient recovered.

DR. ISADORE ROSEN: The lesions on the scalp were not included in the diagnosis of lichen planus. I merely called attention to the fact that this patient has lesions on the scalp in association with this universal eruption of lichen planus of the body. The features of the lesions on the scalp suggest psoriasis rather than lichen planus, and the only way in which one could definitely establish the diagnosis would be by a histologic examination.

A CASE FOR DIAGNOSIS. Presented by DR. J. FRANK FRASER.

R. G., a woman aged 29, single, was employed as a secretary. An eruption developed three years ago with an itching around the waist. This spread to all parts of the body except the face. The cutaneous lesions appeared two years ago as a red eruption. One year ago the patient noticed a swollen gland in the neck. Later other glands became swollen, and one of these was removed from the inguinal region for histologic examination. The patient was seen for the first time today; hence no further data are available.

There is a generalized cutaneous eruption consisting of scalp lesions which suggest psoriasis. In other areas the lesions show infiltration of the borders suggestive of mycosis fungoides.

The patient is presented for diagnosis with a tentative diagnosis of (1) atypical psoriasis and (2) mycosis fungoides.

DISCUSSION

DR. FRED WISE: I think the patient now has mycosis fungoides. Some of the individual plaques are elevated in some segments and flat in others. This is one of the characteristics of the plaque lesions of mycosis fungoides. I think also that the patient had psoriasis and that hers is one of the few cases in which a cutaneous condition begins as psoriasis and becomes "tranformed" into mycosis fungoides.

DR. E. WILLIAM ABRAMOWITZ: I agree with the remarks of Dr. Wise. I think that the patient has mycosis fungoides, but many of the larger lesions on the trunk are covered with overlapping scales and remind one of tinea imbricata.

DR. LUDWIG OULMANN: I agree with the diagnosis of mycosis fungoides, but the fact that the patient is recuperating speaks against this. The patient has gained some weight and has improved without treatment. There are large silvery scales, which indicate that psoriasis was present at the onset.

DR. ANDREW J. GILMOUR: I agree with Dr. Wise, but I think that this patient still has plaques of psoriasis.

DR. ISADORE ROSEN: I am sorry that the presenter did not have the opportunity to undertake a complete study of this case. I do not think that any one can make an absolute diagnosis by the clinical examination alone. If the pathologic findings verify the diagnosis of mycosis fungoides now, the patient undoubtedly had this disease three years ago when the eruption first developed.

DR. FRED WISE: Have any of the members observed geometric cribriform stippling of the nails in any disease other than psoriasis?

DR. E. WILLIAM ABRAMOWITZ: Stippling of the nails should not be considered totally diagnostic of psoriasis. It has been noted in chronic eczematous conditions and sometimes in other cutaneous conditions. It has been reported as occurring after acute rheumatic fever or chorea and after smallpox and other infectious diseases (Rosenau, William H.: Changes in Finger Nails after Rheumatic Fever and Tuberculosis, *J. A. M. A.* **78**:1783 [June 10] 1922). I do not know whether geometric stippling is more significant of psoriasis. In my opinion, hyperkeratosis of the free edge of the nails with yellowish discoloration or destruction of the nails without paronychial inflammation is more characteristic of psoriasis when it involves practically all the finger-nails symmetrically.

DR. DAVID L. SATENSTEIN: I do not believe that this patient has two different diseases, one merging into the other. Microscopic examination would be the only way to establish a diagnosis. There are so many variations in the clinical picture of mycosis fungoides that I feel the way Dr. Fraser does, that a definite clinical diagnosis cannot be made tonight.

DR. MAX SCHEER: I believe that this is a case of mycosis fungoides for the reasons stated by Dr. Wise.

DR. PAUL E. BECHET: In this particular instance it is not easy to make a definite clinical diagnosis. In my opinion, a diagnosis of mycosis fungoides is made too frequently and on insufficient evidence. This belief is borne out by the frequency with which a diagnosis of the prefungoid stage of the disease is made and the comparative rarity of the occurrence of the tumor stage. As an example I wish to cite a presentation which I made before this society on May 8, 1934 (ARCH. DERMAT. & SYPH. **31**:133 [Jan.] 1935). The patient was presented for diagnosis, with a tentative diagnosis of mycosis fungoides. The lesions covered the entire body; they were intensely pruritic, infiltrated and sharply outlined, and one or two of them strongly suggested tumor formation. They had been present for over a year. By almost unanimous opinion the members present at the meeting favored a diagnosis of mycosis fungoides, yet three months later most of the lesions had disappeared without roentgen therapy, administration of arsenic or any of the measures used in the treatment of mycosis fungoides. The eruption recurred a few months later, assuming a picture typical of an allergic eczematoid dermatitis entirely unlike its appearance at the time of presentation. I believe that Dr. Fraser's patient has psoriasis; whether it will or will not develop into mycosis fungoides later on is problematic. In this connection it is proper to state the well known fact that mycosis fungoides may occur on patches of psoriasis which persist for years. Such a case was observed by Dr. Howard Fox in a patient of his father's, in whom typical lesions of mycosis fungoides developed on a psoriatic patch which had been under observation for about twenty years.

DR. J. FRANK FRASER: I am sorry that I was unable to prepare more data. I saw the patient for the first time today. The case will be thoroughly investigated.

DR. FRED WISE: Eight or ten years ago Dr. MacKee and I presented a patient from the Vanderbilt Clinic who had had typical psoriasis for from ten to fifteen years before the appearance of mycosis fungoides. The lesions of the latter disease sprang up at the identical sites at which the psoriasis had occurred.

DR. DAVID L. SATENSTEIN: In these cases psoriasis has not developed into mycosis fungoides. The fundamental pathologic processes of these two conditions are in no way related. Why cannot a patient with psoriasis acquire mycosis fungoides as well as a patient with any other disease? The two diseases are entirely different.

SECONDARY SYPHILIS WITH UMBILICATED LESIONS. Presented by DR. MAX SCHEER.

H. M., a woman aged 44, first came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 8, 1935, with an eruption of three weeks' duration. She presents an eruption which involves the entire body. The individual lesions are discrete and confluent erythematous papules. Many of them are covered with adherent hyperkeratotic scales. Some of the lesions are pustular. The lesions on the palms and soles are similar but are larger and have a central umbilication. The scalp presents elements identical with those over the body. The patient states that there has been a considerable loss of hair since the onset of the eruption. On the face there are numerous bluish-red macules of varying size. The Wassermann reaction of the blood was 4 plus.

DISCUSSION

DR. FRED WISE: The depression in the center of some of the papules should be noted. This type of eruption was frequently seen ten or fifteen years ago.

CHRONIC LICHENOID ECZEMA OF THE LOWER EXTREMITIES IN A DIABETIC PATIENT. Presented by DR. FRED WISE.

This woman, aged 51, was born of Irish parents in Paterson, N. J., where she had resided all her life. She was under the care of Dr. J. J. Greengrass, of Paterson, N. J. She was married twenty-seven years ago; seven years later her husband died, at the age of 35, from cirrhosis of the liver; she has remained a widow for the past twenty years. She has been a teacher since 1905, except during the seven years of her married life. Her father died at the age of 50 of pneumonia; her mother, at the age of 42 of "blood poisoning," and her sister, at the age of 5 of diphtheria. There were no other brothers or sisters. Her four grandparents immigrated to this country and died at advanced ages of causes unknown to the patient. There is no history of familial or hereditary diseases. There is no history of allergic conditions either in the patient or in her family. The patient had measles and mumps in childhood. At the age of 10 she suffered from "eczema" involving both feet, which lasted about four months, disappeared spontaneously and did not recur. One year ago she had a "streptococcic sore throat." She had varicose veins since 1918, with swelling of both legs, on standing. She has had no surgical operations and no venereal diseases. Her menses began at the age of 10, with an interval of twenty-four days and a duration of from four to five days. The menstrual bleeding was always considerable; there was no abdominal pain or backache. The menopause occurred gradually at about the age of 41, and no attendant symptoms were noted. The patient had three pregnancies resulting in three uncomplicated deliveries. Her three children are 26, 25 and 20 years of age and are living and well. Her habits have always been good. Her diet has been varied; she is a heavy eater and is extremely fond of sweets. For the past five years only she has been a moderate smoker and has used alcoholic beverages only occasionally and in small amounts. She takes about three cups of coffee daily, all for breakfast. Her average weight in adult life was about 200 pounds (90.8 Kg.) until four months ago, when in a short space of time she lost 45 pounds (20.4 Kg). Her present trouble consists of local lesions and symptoms of diabetes.

Eighteen years ago the lesions first appeared on the inner aspect of the lower third of both legs as a small erythematous macular lesion about the size of a half-dollar. These areas extended slowly to involve the inner aspect of the lower two thirds of both legs. With this extension desquamation began to appear, and after about five years multiple superficial fissures formed. Part of the area healed, leaving brownish pigmented patches, and extension occurred solely from the margins. The healed areas subsequently became reinvolved. Itching has been a prominent symptom. During the winter the fissures and scaling were more extensive, and

a serous fluid oozed from the openings. During the summer the scaling disappeared, leaving a fiery red area with a sharp line of demarcation.

About six months ago, the patient first noticed the onset of polydipsia, polyuria, nocturia, loss of weight, asthenia, pruritus vulvae and disturbances of vision. She did not know she had diabetes before her examination on Dec. 27, 1934.

A Case for Diagnosis (Tertiary Syphilis? Tuberculosis? Lichen Planus-Like Lesions on the Wrist). Presented by Dr. Isadore Rosen.

C. B., a woman aged 43, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has an eruption of two years' duration on the back of the left leg. She wore a plaster cast for ten weeks before coming to the clinic. The lesion, which measures about 4 by 5 inches (10 by 12.7 cm.) is serpiginous with central scarring and an active advancing purulent border. There are also several umbilicated papules with shining surfaces on both forearms.

Tests with tuberculin gave the following results: with 1:1,000,000 dilution, 1 plus; with 1:100,000 dilution, 2 plus; with 1:10,000 dilution, 4 plus. The Wassermann and Kahn reactions were negative. A biopsy on material from the arm showed a mild degree of sclerosis, no lichen planus and no syphilis. Histologic examination of tissue from the leg revealed a vasculitis and perivasculitis; there was no evidence of lichen planus or syphilis.

DISCUSSION

Dr. George C. Andrews: The character of the lesions, the ulceration, the duration, the tendency to heal in one place and break out in another, all suggest tertiary syphilis. I think the patient should be treated for syphilis in spite of the negative Wassermann reaction.

Dr. E. William Abramowitz: I believe that this patient has a tertiary sepiginous ulcerated syphilid in spite of the single negative Wassermann reaction. There has been some improvement from the local application of mild mercurial ointment. However, the case will be investigated further to exclude some form of tuberculosis of the skin.

Dr. Fred Wise: I regard the lesion as a form of cutaneous tuberculosis or tuberculid, possibly an aberrant form of Bazin's disease.

Dr. Paul E. Bechet: I agree with Dr. Wise.

Dr. Isadore Rosen: This case does not coincide with my clinical conception of Bazin's disease. The age of the patient, the extent of the lesion and the limitation to one extremity are against the diagnosis of Bazin's disease. I believe that the patient has a low grade infection, other than syphilis or tuberculosis, involving the superficial and deep blood vessels.

Lupus Erythematosus Disseminatus. Presented by Dr. Isadore Rosen.

M. S., a woman aged 58, was previously presented at the meeting of the Atlantic Dermatological Conference on Nov. 17, 1934, by Dr. George M. MacKee.

DISCUSSION

Dr. Fred Wise: I saw this patient when she first came into the hospital several months ago. My diagnosis at that time was lichenoid scleroderma. When I examined the patient tonight I realized that I made a mistake in the diagnosis. She has improved tremendously under the injections of a bismuth preparation, but that fact in itself is not proof that the eruption is lupus erythematosus. As yet not much is known about the response of diseases of unknown etiology to bismuth preparations and other medications. Nevertheless, I believe that tonight the appearance of the lesions on the dorsa of the hands is strongly suggestive of lupus erythematosus.

ULCERATIVE CUTANEOUS TUBERCULOSIS? ECTHYMA? Presented by DR. FRED WISE.

B. P., a man aged 45, first came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Oct. 27, 1934, with an ulceration of the left leg of about one month's duration. He stated that in July 1934 a cutaneous eruption developed which was diagnosed as due to poison ivy; it involved both legs and the abdomen up to about the waist-line. He was given some sort of yellow salve for this. About one month after the onset of the eruption ulcerations developed on the anterior aspect of each leg. The ulcers were about the size of a 25 cent piece, and after about sixteen days they were almost healed. The patient states that he sustained a minor injury on the left leg which caused the ulcer to reopen and that he has been in bed for the last two weeks because of this. At present he presents over both shins purplish, depressed ulcerating areas from the size of a dime to that of a half-dollar. There is an indurated palm-sized area on the anterior aspect of the lower portion of the right leg with a central, quarter-sized, punched-out ulceration and a red, gummy-appearing base. The trouble has been present for about four months.

The Wassermann test was negative on two occasions. The patient showed hypersensitivity to tuberculin given intradermally. The biopsy showed a chronic dermatitis with ulceration.

DISCUSSION

DR. MAX SCHEER: The patient did not respond to any treatment until finally bismuth and iodides were given. The lesions then improved a great deal. In spite of the negative results of serologic and histologic examinations, I think this eruption is syphilitic.

DR. GEORGE C. ANDREWS: I gained the impression that the patient has some systemic condition. His color is pasty; he is short of breath. He may have diabetes or some other condition. He says that he has considerable itching of the leg, where the indolent furuncles are located. I think a general medical work-up should help this man.

DR. DAVID L. SATENSTEIN: I do not think that there are enough data on which to base a diagnosis. The lesions certainly do not look like syphilitic lesions.

DR. ANDREW J. GILMOUR: I think the patient has a low grade pyogenic infection.

DR. MIHRAN B. PAROUNAGIAN: I agree with Dr. Gilmour. I advise that the patient be put to bed, that the leg be elevated and that compresses wet with saline solution be applied.

DR. PAUL E. BECHET: Papulonecrotic tuberculid should be ruled out before a specific diagnosis is made.

DR. FRED WISE: I agree with Dr. Andrews that a general physical work-up should be made in all cases of this type. I exclude syphilis in this eruption not only on account of the negative serologic tests, but because the lesions do not convey to me the picture of gummas.

NONFILARIAL ELEPHANTIASIS OF THE SCROTUM. Presented by DR. ISADORE ROSEN.

E. C., a man aged 75, is a patient from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. The external genitalia are enormously swollen. The scrotum is moderately thickened and edematous, attaining the size of a grapefruit. The penis is distorted owing to the chronic edema. Examination showed that the scrotal contents were normal. There was no disease of the inguinal glands. The prostate was normal in shape and consistency. The patient states that he had syphilis forty years ago and was treated by oral administration of mercury.

The Wassermann and Kahn tests were negative. The urine was normal. Examination of the blood was negative for Filaria on Jan. 5, 1935. The biopsy showed chronic lymphedema with eczematization.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: This patient has been treated with dressings moistened with boric acid and has shown considerable improvement in the last few days. In order to exclude the possibility of filarial infection, one would have to make several examinations of the blood, of which at least one should be done at around midnight. I believe that the patient has a chronic lymphangitis of the type of solid edema that has been reported as occurring on the face, hands and legs and that in this instance the condition is probably due to a chronic infection associated with the eczema of the scrotum.

DR. ISADORE ROSEN: I think the only way to treat this patient is to hospitalize him and to examine his blood at night for Filaria. A thorough physical examination for evidence of a primary focus of infection in the perineal region should also be made.

A CASE FOR DIAGNOSIS (LEUKEMIA CUTIS?). Presented by DR. MIHRAN B. PAROUNAGIAN.

Mr. G., an Italian aged 64, had been a cook. His condition began about five months ago while he was destitute and was sleeping on the docks. He thought he had vagabonds' disease, and he applied kerosene. The lesions appeared in the axillary regions and spread rather rapidly to the other portions of the body. They have always been markedly pruritic and at times have been extensively infected secondarily. The patient states that he had no cutaneous disease before this condition appeared.

The lesions are scattered extensively over the body but tend to show grouping on the legs, the upper inner aspects of the thighs, the lower portion of the back, the scapulae, the lateral thoracic wall, the inner aspects of the arms and the nape of the neck.

The lesions are definitely polymorphous, and one can still distinguish active erythematous, fleshy papules, papulovesicles and numerous dark brown pigmented macules.

The Wassermann test and examination of the urine gave negative results.

The results of blood counts were as follows:

	Nov. 2, 1934	Nov. 7, 1934	Dec. 31, 1934	Jan. 7, 1935
White cells	37,500	26,050	22,400	19,650
Red cells	4,000,000	3,500,000	3,470,000	2,830,000
Hemoglobin	80%	75%	65%	79%
Polymorphonuclears	84%	97%	86%	89%
Lymphocytes	12%	2%	6%	4%
Eosinophils	4%	1%	6%	3%
Myelocytes	...	...	2%	...
Premyelocytes	...	...	...	1%

There were some basophilic stippling of the red blood cells and a slight anisocytosis. The picture shown by the blood suggested the incipient stages of leukemia. The condition has improved under palliative treatment; the itching has considerably subsided. The liver and spleen are enlarged.

DISCUSSION

DR. ISADORE ROSEN: I am not convinced that the cutaneous manifestations presented by this patient have any connection with leukemia. There are many follicular pustules on the involved area, and the remaining lesions are pigmentations, the result of the healing of the same type of lesion. The man is healthy-looking and active and does not give the impression of one suffering from such a grave disease.

DR. GEORGE C. ANDREWS: I do not think that any diagnosis other than myelogenous leukemia is correct in view of the blood count and the enlargement of the

spleen and liver. One count showed 98 per cent polymorphonuclears and only 2 per cent lymphocytes. Many counts showed myelocytes. The appearance of the indolent bluish-red nodules in the skin is also characteristic. Leukemia is the only disease that I know of in which one can have a leukocytosis of 25,000 and walk around feeling perfectly well, as this man does.

DR. E. WILLIAM ABRAMOWITZ: Judging from the results of the blood counts this man has leukemia either of the myelogenous or of the mixed myelogenous lymphatic type. The eruption on the trunk may be incidental or toxic.

ADENOMA SEBACEUM. Presented by Dr. LUDWIG OULMANN.

F. R., aged 22, says that seventeen years ago he fell through a window on top of a screen which he held in his hands. He sustained a cut in the middle of the forehead which left two keloidal, walnut-sized scars at the hairline. Some time later convulsions developed; these became less frequent gradually. For the past several years he has had a slowly advancing optic atrophy. His mentality has always been normal.

Eight years ago there appeared a number of brownish-red nodules on the nose and around the nose on the cheeks, and pinhead-sized areas of telangiectasia, some of which were also located on the chin. The patient states that at times a number of those nodules disappear but that with each new outbreak they increase in number. Sebum can be expressed from some of them. Fibrous warts are present on the toe-nails and on one finger. Roentgen examination of the skull revealed a shadow at the base, in the back. The pineal gland was distinctly visible but not enlarged.

DISCUSSION

DR. FRED WISE: I again wish to call the attention of the members to the presence of the small fibromas at the free edges of the toe-nails of this patient, an evidence of the syndrome called morbus Pringle by the Continental dermatologists. Possibly this patient also has tuberous sclerosis; the presence of a tumor at the base of the skull possibly points to the condition described by Hartdegen and Bourneville.

PAUL E. BECHET, M.D., *Chairman*

Feb. 12, 1935

MIHRAN B. PAROUNAGIAN, M.D., *Secretary*

A CASE FOR DIAGNOSIS (ERYTHEMA NODOSUM?). Presented by DR. ANDREW J. GILMOUR.

B. W., a woman, aged 35, was born in Hungary. In 1930 she suffered a nervous breakdown and was bedfast for two years. She was treated with bromides and phenobarbital. She stated that she was "worried and nervous" and that her menses lasted an entire week. She also stated that many Wassermann examinations had been made and had given negative results. There was no history of rheumatism. Before August 1934 she had taken large quantities of bromides, but she had taken none since that date.

In January 1935 a "lump" developed suddenly, appearing overnight. It showed and still shows evidence of soreness when the patient stands or walks for long periods. The lesion is situated on the outer aspect of the middle third of the right leg; it measures ¾ inch (1.9 cm.) in diameter and is barely visible above the surface. The skin is not red, hot or discolored. The lesion is extremely tender to the touch.

The patient is presented for diagnosis. The possibility of erythema nodosum or of an eruption due to ingestion of bromide is suggested.

DISCUSSION

DR. MAX SCHEER: The patient presents lesions which show an active process on the right shin and left calf. The scars on the left calf are suggestive of erythema induratum. The point in the history is that the patient has taken bromides for a nervous breakdown. I think that she has an eruption due to a drug.

DR. HOWARD FOX: The scars on the calf suggest erythema induratum. The nature of the other lesion, however, is uncertain. It is true that erythema nodosum can be caused by bromides, but I hesitate to make a definite clinical diagnosis from this single lesion.

A CASE FOR DIAGNOSIS (POIKILODERMA ATROPHICANS VASCULARE?). Presented by DR. DAVID L. SATENSTEIN.

E. Y., a youth, aged 19, born in Jersey City, N. J., came to the clinic for cutaneous diseases of the Medical Center of Jersey City complaining of discolorations on the body. The condition started seven years ago as small, round, slightly raised reddish-brown lesions which slowly grew peripherally. At no time have there been any subjective symptoms.

The family history and the past history were irrelevant except for the fact that the patient had an abscess on the neck when he was a child and influenza five years ago. He has never been exposed to roentgen rays.

At present the patient has seven fairly large, more or less round lesions, varying from 3 to 5 inches (7.6 to 12.7 cm.) in diameter. The lesions appear on the chest and abdomen and in the right axilla; there are two in the right inguinal region and two on the back. They are well defined and depressed below the level of the surrounding skin; they vary from tan to slate color and are spotted with small white areas, and in some parts they show atrophy. Throughout the lesions there is a moderate amount of telangiectasia.

The Wassermann test and the urinalysis gave negative results. The biopsy revealed the end-stage of a sclerotic process with partial degeneration of the elastic tissue.

DISCUSSION

DR. HOWARD FOX: All the members have seen a few cases like this one, though such cases are unusual. Some would class this condition as the atrophic stage of scleroderma, a conception which does not seem reasonable to me. In some of these cases of long duration there is never any hide-bound infiltration at any time to suggest scleroderma. The eruption is apparently neither a rash due to a drug nor parapsoriasis. There are simply large pigmented and atrophic patches which may be classed as atypical poikiloderma, though they do not present the classic appearance of a dermatitis due to roentgen rays. I can only designate them patches of diffuse atrophy with pigmentation.

DR. MAX SCHEER: I think the eruption is scleroderma.

DR. LUDWIG OULMANN: I am inclined to accept the diagnosis of poikiloderma atrophicans vasculare more than any other. There are progressive patches with pigmentary atrophy and distinct telangiectasia. The histologic examination does not show clumping cells or subepidermal edema, and I advise that another section be examined, but on the basis of the clinical findings I should make a different diagnosis.

DR. PAUL E. BECHET: I have had the good fortune of seeing several cases of typical poikiloderma atrophicans vasculare. The clinical picture presented by Dr. Satenstein's patient is entirely different from that of poikiloderma. On the other hand, it is strongly suggestive of morphea, and I therefore prefer the latter diagnosis.

A Case for Diagnosis (Mycosis Fungoides?). Presented by Dr. Isadore Rosen.

This patient first came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 9, 1934, complaining of an intense generalized pruritus. The condition began on the fingers four years ago. A few months later the nape became involved. A remission occurred during the summer of 1931, but in the autumn of that year the itching became generalized and did not respond to topical therapy. There is a generalized, dry, moderately lichenified and furfuraceous erythroderma. There are many scattered linear crusted excoriations. There has been a gradual progressive, diffuse loss of hair from the scalp since the onset of the illness. The studies of the blood gave the following results: hemoglobin, 106 per cent; red cells, 5,900,000; white cells, 10,000; polymorphonuclears, 33 per cent; lymphocytes, 56.5 per cent; mononuclears, 4 per cent; eosinophils, 5.5 per cent, and basophils, 1 per cent. The sugar content was 133 mg. per hundred cubic centimeters of blood.

A report on a biopsy (Feb. 1, 1935) by Dr. Satenstein was as follows: Throughout the upper portion of the cutis there is a moderate diffuse cellular infiltrate, which is partly arranged in focal masses. The epidermis is in part irregularly acanthotic; the granular layer is retained throughout but composed of cells. The cellular infiltrate is composed of small round cells, wandering connective tissue cells and some epithelial cells. Between the cellular elements there is a fine reticulum. There are some mitotic figures and clumping of nuclei.

The diagnosis based on the microscopic examination is: possible mycosis fungoides.

DISCUSSION

Dr. Ludwig Oulmann: I did not see the microscopic section in this case. Clinically the condition appears as pityriasis rubra of Hebra to me. The patient complains of constantly feeling cold and chilly when he undresses. He is losing hair from the scalp and eyebrows, and the infiltration in his erythroderma is not marked. The glands do not present the appearance associated with Hodgkin's disease. As many of the patients with this condition finally die of tuberculosis, I should like to know whether a tuberculin test has been made.

Dr. Henry J. F. Wallhauser, Newark, N. J.: I favor the diagnosis of pityriasis rubra on account of the generalized hyperemia associated with a peculiar copper color and with moderate scaling and scattered elevated keratotic lesions. Further observation, however, regarding the clinical course will be necessary to establish this diagnosis.

Dr. J. Frank Fraser: I agree with Dr. Oulmann. The features seen tonight lead me to believe the condition is pityriasis rubra of Hebra.

Dr. Howard Fox: Whether one calls this patient's disorder pityriasis rubra of Hebra, dermatitis exfoliativa or universal scaling erythroderma, it is a type of eruption in which the possibility of lymphoblastoma should be suspected. A definite diagnosis cannot be made clinically. In some cases of this type histologic examination shows the condition to be psoriasis.

Dr. Max Scheer: I agree that a diagnosis cannot be made on clinical findings alone. It is necessary to make a biopsy and a cell count. The eruption is an erythrodermic type of mycosis fungoides which may remain erythrodermic for a long time.

Report on a Case Previously Presented. Dr. J. Frank Fraser.

The complete history and report of laboratory findings in the case of R. G., presented before this society in January (Arch. Dermat. & Syph. **32**:324 [Aug.] 1935) are as follows: The report from St. John's Hospital stated that a blood count made in September 1933 showed 4,000,000 red cells, 6,100 white cells, 58 per cent polymorphonuclears, 30 per cent lymphocytes, 6 per cent monocytes and

6 per cent eosinophils. The hemoglobin content was 72 per cent (10.5 Gm. per hundred cubic centimeters of blood).

The urinalysis at that time showed no changes other than a trace of albumin and a few red cells.

The results of a microscopic examination of an inguinal lymph node by Dr. Curphey were reported as follows: "There is marked alteration of the architecture of the node. The reticulum cells are hyperplastic. In certain areas these cells have neoplastic features, as evidenced by hyperchromatism of the nodular structure and anaplasia. Occasional mitotic figures and large mononuclear cells with lobulated hyperchromatic nuclei resembling Sternberg-Reed cells are seen. The number of lymphocytes is relatively reduced. The germinal follicles are hyperplastic. The microscopic picture is that of a lymphogranulomatous process having microscopic features of both lymphosarcoma and Hodgkin's disease and for that reason may be described as Hodgkin's sarcoma. In order to rule out the related diseases in this group it would be necessary to make a careful study of the blood for evidence of any leukemic process."

A roentgenogram taken on September 27 showed diffuse bilateral peribronchial adenitis with some calcified glands scattered throughout both pulmonary fields and having the appearance of healed or nonactive tuberculosis.

The patient was examined at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 19, 1934, and the diagnosis made there was exfoliating dermatitis. The histologic report on a section of skin was dermatitis. The histologic structure of a section of skin removed on March 6 substantiated the clinical diagnosis of psoriasis. There was no histologic evidence of mycosis fungoides. The patient was given seven roentgen treatments of ¼ unit (75 roentgens) on the face, and marked improvement occurred.

A biospectrometric analysis by Dr. Gaul showed that the metallic elements except chromium were present in normal quantities.

The density of the line for chromium indicated a retention of chromium corresponding to the retention of nickel as found in cases of psoriasis.

The findings as to chromium were considered significant in that this case represents an aberrant clinical picture of psoriasis and chromium and nickel have the same chemical and physical properties. (The term "biospectrometric analysis" refers to a quantitative spectrographic analysis for the metallic constituents in differentiated and undifferentiated mesoderm, obtained by taking with a 0.47 cm. punch a dermal specimen for biopsy weighing approximately 0.025 Gm.)

DETROIT DERMATOLOGICAL SOCIETY

G. Warren Hyde, M.D., *Recorder*

Regular Meeting, Jan. 15, 1935

Clyde K. Hasley, M.D., *Presiding*

Neurotic Excoriations. Presented by Dr. R. C. Jamieson.

Case 1.—S. B., a man aged 52, unemployed, has multiple excoriations on all parts of the body; evidently the lesions have been present for a long time. They may be based on urticaria, prurigo or a neurosis. The excess pigmentation is suggestive of some endocrine change, possibly related to the adrenal glands. The ulcerations on the legs appear to be due to excoriations with secondary infection. Examination of the blood showed 50 per cent hemoglobin and 3,010,000 red blood cells. The Kahn reaction was 4 plus. Culture of material from a lesion showed Staphylococcus aureus.

GENERALIZED DERMATITIS OF ECZEMATOID TYPE, POSSIBLY ON AN ALLERGIC BASIS. Presented by Dr. R. C. Jamieson.

CASE 2.—J. K., a student aged 20, presents a generalized eczematoid dermatitis with many marks of scratching. He also has asthma which recurs every fall. Examination of the blood showed 70 per cent hemoglobin, 3,260,000 red blood cells and 20 per cent eosinophils. The Kahn test was negative. Cutaneous sensitization tests gave negative results with egg white, egg yolk and oats.

ALLERGIC DERMATITIS. Presented by DR. ROBERT C. JAMIESON.

CASE 3.—This housewife, aged 26, had no cutaneous disorder until a few weeks ago, when suddenly there developed a severe pruritus followed by the generalized dermatitis which the patient now exhibits. The dermatitis is of the eczematoid type. Wherever the patient's hands can reach there are marks of scratching.

DISCUSSION

DR. CLAUDE W. BEHN: I think these are three interesting cases, although I cannot satisfy myself that the condition exhibited by the patient in case 1 should fit in with that of the patients in the other two cases. I think that the patient in case 1 presents an ulceration on the legs with secondary infection and pigmentation. The body shows deep pigmentation. It may be that the disorder is associated with some metabolic condition, possibly, as Dr. Saunders suggested, with dysfunction of the adrenal glands, perhaps carcinoma. The other two cases, I think, fall into the group of allergic dermatitis, associated perhaps with an endocrinopathy or some psychogenic factor. Treatment should be along these lines. I do not believe that local treatment alone will bring about a cure.

DR. R. A. C. WOLLENBERG: I agree with Dr. Behn. In cases of toxic disturbances of long standing, itching is commonly found. In order to know what causes it, I should want to know more about the individual cutaneous lesions. Fifty per cent hemoglobin suggests a number of things. There are many causes of blood dysplasia which may be important factors. So far as the pigmentation is concerned, it could no doubt be explained on an endocrine basis. Long periods of scratching may produce this type of condition. It may be purely a phenomenon due to hysteria. The case requires a great deal of study. The other two patients' disorders may be classed as allergic eczema.

DR. LOREN W. SHAFFER: I agree that the conditions in cases 2 and 3 may belong in the group of allergic dermatitis, while that in case 2, so far as I can see at present, is a dermatitis factitia on a neurotic background or on the background so unsatisfactorily classified as "vagabondi." Disturbances such as those in cases 2 and 3 I have always found extremely difficult to explain. Even after I have studied these cases for years, I still know only a little more about them than I did at the start.

DR. GEORGE VAN RHEE: I saw the patient in case 2 before he entered the hospital, and today I should not recognize the condition because it is much improved. The patient also had a secondary infection when I first saw him. I cannot agree with the other speaker. I think that in case 2 the condition is allergic and that in case 3 seborrheic dermatitis enters as a factor. The patient in case 3 has scaling on the scalp. In case 1 there are, I believe, neurotic excoriations at the present time, and these account for the pigmentation.

DR. ROBERT C. JAMIESON: I presented these patients because in my opinion the cases showed a certain degree of similarity in that in all of them there was a factitious dermatitis, whether intentional or not. In the three patients the back is practically free from lesions. In case 1 the positive Wassermann reaction and the secondary infection, I think, merely obscure the picture. This patient has a low grade of mentality. He has had hemiplegia for a number of years and also intense itching. The itching began without a lesion; the amount of pigmentation he exhibits is seen in cases of severe pruritus. The patient's skin is dark, and I think

that his is a case of pruritus, the pigmentation following prolonged scratching. The patient may later show a disturbance of the adrenal glands. The patient is an Austrian, and the condition may have started as prurigo. The whole picture of the cutaneous lesions may be explained on a psychogenic basis.

The lesions in case 2 do not look at all as they did when I first saw the patient. He had excoriations of long standing, not a dermatitis of the eczematoid type. In this case again the lesions are on the face, upper part of the shoulders, arms and legs. The patient has been at the Eloise Hospital for Mental Diseases, and sensitization tests were negative. During his sojourn in the hospital he has had no treatment he had not had before. He has had baths with colloidal substances, and his diet has been restricted with regard to proteins, meat and eggs. In case 2 there is a possibility of a psychogenic element. The patient's father committed suicide. Previously the young man had no cutaneous trouble; he was used to eating every kind of food without ill effects, and then, apparently without any forewarning, a rebellious eczematoid eruption developed. In the inguinal region and in both axillae large masses appeared. These may develop into lymphoblastomas later.

The patient in case 3 states that she was entirely free from any eruption up to a short time ago, and she now exhibits a true allergic dermatitis due to some contact, the nature of which she has not been able to determine. Most of her lesions are due to contact, the exciting factor being transmitted by the patient's fingers.

A Case of Anomalous Pigmentation. Presented by Dr. Robert C. Jamieson.

Adele M., a student aged 18, exhibits an increasing amount of bluish-black pigmentation on the eyelids and surrounding areas of the forehead, temples and cheeks. Portions of the sclerae show similar pigmentation. The condition was first noticed about five years ago. The pigmentation on the eyeballs has been present since infancy. The retinas show finely granular pigmentation which is dense near the macula and fades toward the periphery. The color field for blue is slightly diminished.

DISCUSSION

Dr. Harther L. Keim: This case is unusual. I do not recall ever having seen anything even comparable to the condition presented by this patient. In spite of the fact that it has been present since infancy, I am inclined to believe that the pigmentation is due to localized argyria following the administration of a silver preparation in infancy. The color is certainly that seen in cases of argyria so far as the pigmentation of the skin is concerned. I have seen it in the conjunctiva, but the bluish discoloration present in both eyes leads me to believe that the application of the silver preparation to the eyes after delivery, together with an unusually large amount of some peculiar lymphatic drainage, may be at least one explanation for this unusual pigmentation.

Dr. Cyril K. Valade: I think that this case is interesting. This condition may occur in an adult. I remember seeing an adult who had a pigmentation of this type. He acquired his condition from using mild silver protein. He had considerable difficulty in seeing.

Dr. Robert C. Jamieson: When I saw this patient I believed at first that the condition was argyria, but after going into the history a little more carefully I changed my mind. The color of the pigmentation is, of course, extremely suggestive of argyria. It seems a little unusual that after the application of silver nitrate in infancy a pigmentation of the skin should develop after a lapse of twelve or thirteen years. Should the condition be ascribed to the application of silver, or should it be classified as a variety of nevoid formation? Since I saw this patient last the condition of the skin around the eyes is, I believe, definitely lighter.

Dr. William G. Saunders: The slaty blue color present in cases of argyria is lacking. The pigmentation is more circumscribed, and I favor a diagnosis of a nevoid lesion.

Dr. Claude W. Behn: I agree with a diagnosis of argyria, but I cannot see how the pigmentation could be carried into the retina just the same as it could be carried out of the conjunctiva into the skin. A mistake might have been made in applying the silver preparation to the eyes of the infant; the solution might have been too strong. I also believe that argyria may last throughout life. On the other hand, a mild solution may produce the same effect. I saw a woman last month in whom the same condition developed.

A Case of Lichen Planus Bullosus (?). Presented by Dr. Cyril K. Valade.

S. B., an American housewife aged 40, was seen in November 1934 with a condition which was diagnosed as mild epidermophytosis between the toes. It has responded to local therapy.

On Jan. 8, 1935, the patient presented a generalized erythematous scaly, vesiculobullous eruption assuming various shapes and involving especially the neck and flank and the upper and lower extremities. Some of the lesions were scaly; others were vesicular and followed marks of scratching. Some of the lesions along the flank and ankles were bullous. The patient was not ill, although the itching was most distressing. Soothing therapy was prescribed.

On January 11 the eruption had the same distribution, but the character of the lesions had changed to groups of small glistening papules and plaques. The latter occurred at the site of the former vesicles and bullae. No biopsy has been made as yet.

DISCUSSION

Dr. Howard J. Parkhurst: From the grouping of the lesions around the hips, and especially since the pigmentation is pronounced, I believe that the disease may be a dermatitis herpetiformis. I could find no vesicles or bullae, although Dr. Valade assured me that such lesions had been present.

Dr. Cyril K. Valade: The patient has improved considerably since I first saw her a week ago today. From the history she has had the eruption for four weeks. The vesicles were located on the hands and around the ankles, and a few were present on the flank. Most of the lesions were irregularly shaped. There were scaly areas which at that time I believed to be lesions of pityriasis rosea. Last Friday some of the members and I saw the patient together. At that time the characteristic lesions were definitely small rectangular vesicles and papules, and there were large plaques on the wrists and ankles. We thought then that a diagnosis of lichen planus bullosus should be considered.

Dr. Harther L. Keim: One condition suggests itself to me, and I offer that diagnosis as one of the outside possibilities, namely, the Senear-Usher syndrome. At times that disease goes through a peculiar conglomeration of lesions representative, so to speak, of various conditions.

Dr. R. A. C. Wollenberg: I am much inclined to believe that the condition is dermatitis herpetiformis.

Syphilis, Papular Secondary. Presented by Dr. R. Dixon.

L. L., a Negro maid aged 21, single, complains of headache, backache and pain in the side and chest. These symptoms have been present since Dec. 23, 1934. A few papules appeared on December 25. There are no lesions on the face, hands or genitalia. The patient was vaccinated fourteen years ago.

DISCUSSION

Dr. Robert C. Jamieson: I agree that the patient presents one of the common types of papular syphilid. Before eruptions of this type are seen the patient has usually undergone treatment for scabies. I think this is the first case which I have ever seen in which corymbose lesions occurred on the elbow and macular lesions appeared on the trunk in the same patient at the same time. I do not recall having seen these manifestations together before. The girl has had heachache, backache

and coryza and also pain in the side and chest. She became ill December 23, and the lesions broke out on December 25. Other lesions have appeared in succession, those on the lower extremities apparently preceding those on the upper. There are no lesions on the palms, soles, face, neck and genital region. The diagnosis by the diagnosis division of the Board of Health was chickenpox.

DR. WILLIAM G. SAUNDERS: The development of the lesions appears much like that seen in cases of molluscum contagiosum. There was a white papule, and, in my opinion, the generalized eruption is suggestive of smallpox. The absence of lesions of the face and the history agree well.

A CASE FOR DIAGNOSIS. Presented by DR. ROBERT C. JAMIESON.

W. D., a married man aged 38, is unemployed at present. Three months ago a number of brownish-red maculopapular lesions appeared on the central portion of the forehead and on the nose and adjacent portions of the cheek; one lesion appeared on the thigh and one on the trunk. There is no pruritus. At times the lesions are less pronounced, but they recur. They vary in size from 3 to 7 mm. in diameter and are slightly elevated and not scaly. The mucous membranes are not involved. The Wassermann reaction was negative. There is no history of any medication. Toxic erythematous eruptions have been present occasionally.

DISCUSSION

DR. ROBERT C. JAMIESON: The appearance of the lesions as presented today varies considerably from that up to four or five days ago. The patient had a primary syphilitic infection eight years ago. He received treatment immediately. The lesion cleared up; the blood never showed a positive reaction, and the patient never had other symptoms. He has received no treatment since the first year. A week ago lesions appeared on the forehead, nose and adjacent areas of the cheeks. There were no scaling and no itching. In view of the preceding history it seems that the eruption may be a late maculopapular syphilid. The lesions have been present for three months without change, except for slight variations from time to time. The Wassermann reaction was negative. If this is a late maculopapular eruption of secondary syphilis the interval between its appearance and that of the primary lesions is the longest I have recorded.

DR. HOWARD J. PARKHURST: The lesions are clearcut and not particularly indurated or infiltrated. They impressed me as being lesions of lupus erythematosus.

DR. G. WARREN HYDE: I do not think that the eruption is a manifestation of secondary syphilis. It has always been my impression that an eruption of secondary syphilis is generalized. This patient's lesions resemble those of lupus erythematosus, as Dr. Parkhurst said. There is no follicular plugging.

PHILADELPHIA DERMATOLOGICAL SOCIETY

VAUGHN C. GARNER, M.D., *Secretary*

Jan. 18, 1935

ROBERT L. GILMAN, M.D., *Chairman*

DERMATOPHYTOSIS WITH "IDS" (SEBORRHEIC PSORIASIS?). Presented by DR. ABRAM STRAUSS.

W. S. T., a man aged 29, when first seen three months ago presented a large circular, inflammatory, edematous patch on the lower portion of the leg. The scrapings were positive for fungi. Ten days later lesions assumed to be dermatophytids appeared on the upper portion of the arms and legs. Today he has

crusted lesions all over the body and vesicular patches in some places, including the scalp. The soles and interdigital regions show eczematoid ringworm.

Newer lesions presented no fungi in potassium preparations. The original patch and the lesions on the feet were positive for fungi.

Treatment has consisted of roentgen irradiation to the original patch and application of lotion of bismuth and lead to the other involved parts.

DISCUSSION

DR. F. D. WEIDMAN: I want to comment only on the seborrheic factor. The patient does not present a full-blown seborrheic dermatitis, in which connection I have always been sympathetic with Brocq's concept of "mixed dermatosis." For example, it is perfectly clear that this patient has a dermatophytosis; the distribution on the trunk is compatible with dermatophytosis with "ids," and yet there is the other item in the case, namely, seborrhea. Brocq's idea was that when the fully developed disease did not exist but there was nevertheless a tendency in that direction, in the presence of superimposed disease (such as psoriasis in a patient with seborrhea) there would be an intermixture of the lesions of the two diseases. I think that theory may explain the rather yellowish crusted quality of the lesions shown by this patient. That is, there is a dermatophytosis and an "id" in a fundamentally seborrheic subject. I think that perhaps if one keeps in mind the concept of Brocq it will tide over some other difficulties. For example, a dermatosis which is almost ichthyotic, perhaps not a fully developed ichthyosis, complicated by a disease which ordinarily is not hyperkeratotic might under these circumstances be hyperkeratotic.

DR. DONALD M. PILLSBURY: I think that if the eruption is an "id" it may be helpful to do a patch or an intradermal test.

DR. EDWARD F. CORSON: These "ids" are occasionally seen on the extremities, but is it not unusual to find them on the scalp? The presence of similar lesions on the scalp of this patient seriously suggests the possibility of a pustular or seborrheic type of psoriasis or a seborrheic dermatitis.

DR. THOMAS BUTTERWORTH, Reading, Pa.: The appearance impressed me as not that of dermatophytosis but rather as that of seborrheic dermatitis.

DR. S. S. GREENBAUM: The morphology of these lesions is that of the well known nummular eczema. It does not impress me as being that of psoriasis. The scalp is involved to a moderate extent and does not show the scaling and crusting which one would expect to see on a patient with seborrheic dermatitis. Whether or not the underlying factor is a toxic result of the ringworm on the feet is another question. A trichophyton test would only indicate that the patient has had at some time or still has trichophytosis, but it would not definitely prove that his condition is an "id." Clinically it has been my experience that these conditions do not react to the drugs ordinarily used in treatment of ringworm in the way in which they react on the feet.

DR. ABRAM STRAUSS: The original lesion on the leg is typical of ringworm. The lesions that subsequently developed began right above that lesion and in the first week were confined to the leg. They were typical "ids" at that time. The lesions on the arms and body exemplify a still later stage of development; they changed to the form seen tonight within the past week. The patient has received no internal medication.

DR. F. D. WEIDMAN: After the patch test is made the value will reside largely in the readings on the focal rather than on the local lesions. I suggest that after the patch test with trichophytin is made tuberculin be also used.

KERATOSIS FOLLICULARIS (DARIER'S DISEASE), ASSOCIATED WITH VERRUCA PLANA. Presented by DR. ALLEN D. KING.

This well nourished man, aged 34, states that he has a dermatosis of six years' duration. The eruption started over the upper part of the back and presternal

regions and slowly became more extensive. There are no symptoms except occasional mild pruritus. He presents a closely-packed, discrete, reddish-brown follicular eruption sharply localized to the upper portion of the back, the presternal region and the deltoid areas and involving less severely the scalp and the sides of the forehead. The individual lesion was a small follicular keratotic plug or spine. When it was removed the mouth of the follicle remained patulous. There are little inflammatory reaction about the follicles and no atrophy. In addition there are several indolent, flat-topped, noninflammatory papules over the dorsa of the hands and feet, which antedate the other eruption. The Wassermann and Kahn reactions of the blood were negative. All therapy, including application of various ointments and one fractional dose of roentgen rays, was without result.

DISCUSSION

DR. D. M. SIDLICK: The lesions about the ankles appear to be lichen planus, and I think that lesions of similar character are present in the mouth; this leads me to believe that perhaps the condition is the hemorrhagic form of lichen planus, although I have never seen a case of that condition.

DR. HERMAN BEERMAN: The lesions on the ankles as well as some of those on the face were thought to be flat warts.

DR. FRANK C. KNOWLES: My co-workers and I saw this patient some time ago and diagnosed the condition as Darier's disease. There is a curious color to the greasy scale on the lesions which is really characteristic clinically of that disease.

DR. H. J. SMITH: I think the condition is Darier's disease.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I concur in that diagnosis.

DR. F. D. WEIDMAN: The really surprising thing is that even though the disorder has lasted for six years there has not been any confluence of the lesions into patches. The lesions are strikingly individual. I noticed quite a number on the backs of the hands, and there the keratotic material was not pigmented at all; the lesions might be easily overlooked. Many of these lesions were not related to the hair follicles; there might be a hair extending from the lower end of one of the lesions, but some of the lesions were independent even of that. I advise that a biopsy be made, preferably on one of the lesions which appear to be unrelated to a hair follicle.

DR. ALLEN D. KING: A biopsy is being made on a lesion on the back and on one from the ankle.

NOTE.—The biopsy on a lesion from the back showed the classic picture of Darier's disease; that on a lesion from the ankle showed the structure of verruca plana.

DARIER'S DISEASE? ATYPICAL LUPUS ERYTHEMATOSUS? Presented by DR. J. V. KLAUDER.

This fairly well nourished man, aged 51, presents a purplish-blue, elevated, keratotic, slightly scaly, thickened eruption distributed symmetrically over the ears, cheeks, upper lip, neck, tip of the nose and extensor surfaces of the hands. There is a quarter-sized patch on the left undersurface of the chin, with a smooth central depression. On each side of the spinal column there are about four pigmented, irregular, oval, scarred areas. The lesions on the backs of the hands and on the neck are roughened and feel like a nutmeg-grater. The buccal mucosa and the scalp are not involved. The physical examination, including examination of the heart and lungs, gave essentially negative results. The blood pressure was 110 systolic and 65 diastolic. In March 1934 the Wassermann reaction of the blood was negative. A complete blood count gave normal results, and a roentgen examination of the chest revealed no signs of tuberculosis. After five months a guinea-pig which had received an injection of material from the lesions into an

inguinal lymph node exhibited no demonstrable pathologic changes. A biopsy specimen from one of the lesions on the back was reported to show the picture of chronic dermatitis. Sixty injections of gold and sodium thiosulphate, twelve injections of a bismuth preparation and adherence to a salt-free diet for ten months produced marked improvement.

DISCUSSION

DR. D. E. R. GROSS, Wilmington, Del.: I believe this patient was previously presented before this society with a diagnosis of lupus erythematosus and lupus vulgaris. Last week the patient appeared at a clinic for ocular diseases because of loss of vision in the left eye, and the ophthalmologist made a diagnosis of thrombosis of the central artery of the retina. The patient was then sent to the clinic for dermatologic diseases, and it was thought that he had typical lupus erythematosus but that the diagnosis of Darier's disease was also to be considered.

DR. D. M. SIDLICK: The disorder may be tuberculosis.

DR. V. C. GARNER: I subscribe to a diagnosis of lichen planus hypertrophicus.

DR. F. D. WEIDMAN: I was of the same opinion when I saw the patient's hands only, but there are other features of the distribution—those on the face, for example—that did not seem to fit in exactly with that diagnosis. If the condition is lichen planus, it is rather atypical.

DR. S. S. GREENBAUM: The patient has been under my care for about seven months, and when he was first presented before this society the opinion was in favor of a diagnosis of lupus erythematosus, the lesions on the back suggesting lupus vulgaris. Some of the material from these lesions was inoculated into a guinea-pig, but the results were negative, which, of course, does not eliminate the possibility of a tuberculous origin. The patient was given a short treatment with a bismuth preparation followed by about fifty subcutaneous injections of 0.5 mg. of gold sodium chloride administered twice weekly. The oral dose of gold sodium chloride is from $\frac{1}{20}$ to $\frac{1}{10}$ grain (0.003 to 0.006 Gm.) once, twice or three times a day, and the dose that the patient was receiving twice a week is equivalent to $\frac{1}{128}$ grain (0.0005 Gm.). With that medication the blood picture, which showed a marked shift to the left, practically cleared up to such a degree that the pathologist remarked that the indications in the blood of a chronic or subacute bacterial infection were entirely obliterated by the medication. The patient felt well, and although he was on a salt-free diet he was getting sodium chloride with the gold preparation. The condition cleared up fully 80 per cent. The lesions on the ears and dorsa of the hands especially had this thickened appearance, but some of the lesions on the back and some of the lesions on the side of the neck did not show that type of thickening. Ten days ago the patient suddenly found himself unable to see out of the left eye, and I thought that he had a retinal hemorrhage due to a toxic effect of the gold salt on the blood vessels.

An ophthalmologist saw him that morning and made a diagnosis of retinal embolism, which, I understand, is not always easy to differentiate from a retinal thrombosis. The immediate thought was that the gold was responsible for this ocular condition, but on looking over the literature I find that in the many thousands of injections which have been administered Rulison's case is the only instance of retinal embolism that has been reported. I therefore doubt that the gold had anything to do with this complication. The interesting feature of this case, therefore, is the development of an embolism during the course of therapy, rather than the diagnosis.

IDIOPATHIC HEMORRHAGIC SARCOMA OF KAPOSI. Presented by DR. LAWRENCE C. GOLDBERG for DR. JOHN H. STOKES.

This well developed, cooperative man, aged 66, presents a discoloration of the legs which first appeared three years ago. The lesions have grown and become disseminated since their first appearance. The family history is irrelevant. The patient has always been in excellent health. His pulse and temperature are normal.

There is extensive erythema over both lower extremities. Scattered over the legs are many dark purple, reddish subcutaneous plaquelike lesions. Similar lesions are present on the thighs, buttocks, arms, wrists and hands. The mouth shows leukoplakia and sepsis; the heart is normal; the lungs show emphysema; the liver and spleen are not palpable. There is a large, indirect inguinal hernia, and tenderness is present around the anal ring. A roentgen examination of the chest showed no metastases. The gastro-intestinal tract showed no abnormalities when examined after an enema of barium sulphate. The blood count revealed: red cells, 4,600,000; white cells, 8,300; hemoglobin, 112 per cent. The results of the differential and platelet count were normal; the amount of blood urea nitrogen was 10 mg. per hundred cubic centimeters of blood; that of blood sugar, 84 mg. A biopsy was performed. The section demonstrated was not cut from the center of the lesion. There were newly formed blood vessels and a deep infiltrate in the corium. Only local treatment has been given.

DISCUSSION

DR. F. D. WEIDMAN: I agree with the diagnosis. I think that whereas the lesions are not particularly pigmentary, the presence of a notable degree of elephantiasic thickening at the base of the toes and extending onto the dorsum pedis between them is a valuable item in doubtful cases. The presence of lesions on the hands is not rare. It is unusual, though, for the lesions to be seen on the forearms and trunk, as is the case in this patient. The histologic sections were not cut sufficiently deep to be interpreted.

DR. FRANK C. KNOWLES: I should call this patient's condition sarcoma not typical of the Kaposi variety; it presents a curious formation with transverse linear lesions, many of which are separate and distinct rather than grouped.

DISSEMINATE DISCOID LUPUS ERYTHEMATOSUS. Presented by DR. LAWRENCE C. GOLDBERG for DR. JOHN H. STOKES.

This man, aged 32, complains of an eruption which appeared ten months ago behind the ears. It gradually spread to the neck, arms, chest and back. It is moderately pruritic. The patient has lost 20 pounds (9.1 Kg.) in ten months. There are no constitutional symptoms. The family history is irrelevant. The temperature and pulse are normal. Over the face, back, neck, chest, arms and legs there is an erythematous, scaling, telangiectatic eruption. There is some evidence of atrophy over the back and chest. The lesions are discoid. General examination gave the following results: The spleen and liver were not palpable; the heart, lungs, ears, nose, throat and teeth were normal; roentgen examination of the chest and teeth showed no abnormalities. The blood count revealed: red cells, 4,500,000; hemoglobin, 91 per cent; white cells, 5,500. The results of the differential count were: polymorphonuclears, 34; lymphocytes, 57; monocytes, 4; eosinophils, from 2 to 12. There were no abnormal cells. The urine was normal. Serologic tests of the blood were negative. No biopsy was done. The patient was given five injections of 0.5 cc. of tartroquiniobine intramuscularly at two day intervals. Quinine was administered by mouth.

DISCUSSION

DR. F. D. WEIDMAN: I was impressed by the markedly symmetrical character of this dermatosis, by the V-shaped, enormous patch extending over the shoulders like a cape and by the marked involvement of the extensor surfaces as contrasted with the scarcity of lesions on the flexor areas. It makes one think strongly of a toxic factor of the order of erythema multiforme rather than of an actual microorganismal process. I was also impressed by the degree of atrophy at the margins and, for that matter, actually between some of the patches of erythematous infiltration. I appreciate fully that one cannot speak of true atrophy in cases of lupus erythematosus; in areas affected by that disease there is always seen under the microscope a residuum of fibrous tissue; the atrophy is false. In this patient

the areas of "atrophy" are sufficiently large to be picked up between the fingers, and the texture of the skin in those parts seems to be precisely the same as that of the adjoining normal skin. That is, clinically there is little, if any, fibrosis in these places. The involvement appears to be a true atrophy. There are also complete depigmentation and hairlessness in these parts. I should be much interested to learn whether there have been erythematous infiltrations at one time in these particular places. Has the patient had extensive treatment with a gold compound? Could such an atrophic change be ascribed to the therapy?

DR. DONALD M. PILLSBURY: My co-workers and I should be glad to receive any therapeutic suggestions in this case. During the past three or four days some new lesions which were not there a week ago have developed over the flanks and lower part of the back. When the patient came in he stated that he had been exposed to ultraviolet rays.

DR. FRANK C. KNOWLES: I do not think that treatment with a gold preparation should be used in this case. I should give sodium thiosulphate intravenously. I think that will be effective.

DR. F. D. WEIDMAN: One might try a bismuth preparation.

DR. ROBERT L. GILMAN: The patient has received salt of quinine and bismuth.

DR. D. M. SIDLICK: I should say that therapy with bismuth is a complete failure. In the two cases in which I have tried it I did not obtain any results whatever.

DR. DONALD M. PILLSBURY: I think the members all recall the patient who was shown in New York; he responded well to treatment with bismuth.

DR. J. M. SCHILDKRAUT: Some years ago I presented a female patient with disseminated lupus erythematosus of forty years' duration. When gold sodium thiosulphate began to be used I treated her with it, and the condition cleared up entirely.

DR. V. C. GARNER: My co-workers and I are of the opinion that in these cases of disseminate discoid eruptions a gold preparation may be given in exceedingly small doses.

DR. ABRAM STRAUSS: Some years ago I presented an elderly female patient with disseminated lupus which I treated with a gold preparation. The disorder cleared up satisfactorily, leaving areas of vitiligo all over the body. The condition recurred and again cleared up promptly under therapy with a gold preparation, leaving, after both attacks, a residual vitiligo.

DR. FRANK C. KNOWLES: I think there is quite a question whether the eruption in the present case is not of the acute disseminate type. New lesions are appearing, and it seems to me that many of these lesions are extremely inflammatory. My co-workers and I have given a gold preparation to some patients with inflammatory discoid eruptions of this type, and there was not only a marked reaction in the lesions themselves but a marked general reaction. I believe that this patient's eruption is on the borderline between the discoid and the acute disseminated type; with the appearance of the new lesions it seems to lean a little more toward the acute than toward the chronic type, and therefore therapy with a gold compound is contraindicated.

DR. ROBERT L. GILMAN: Tartroquiniobine is a preparation that many of the members would choose in treating lupus erythematosus, as it contains both bismuth and quinine, but the fact that the patient has grown worse under treatment with this preparation may be due to an idiosyncrasy, and I think that one would be justified in using another salt of bismuth before condemning the treatment entirely.

DR. S. S. GREENBAUM: I agree with what has just been said. According to Throne there is a method of determining whether a gold compound in any form when injected may or may not produce a reaction, and this method is based on the chemical findings in the blood, especially on the blood sugar. When the blood

sugar is high one ought to be careful in using injections of a gold compound. There is another element in this case that is interesting. Is the eruption due to quinine, or is it a focal reaction to the injection of a stimulating agent like bismuth? I am quite sure that in many cases bismuth is just as beneficial as gold, and there seems to be no reason why the treatment with bismuth should not be continued for a little while, perhaps in a different form, as Dr. Gilman has suggested. A large part of the eruption may be purely the result of a focal reaction.

DR. FRANK C. KNOWLES: Two contraindications to medicaments containing gold are the presence of an increased amount of sugar in the blood and a decreased amount of chloride. The possibility of such contraindications being present should be investigated in this case.

DR. S. S. GREENBAUM: Many dermatologists are afraid to use injections of a gold preparation in cases of extensive eruptions.

DR. EDWARD E. CORSON: I recently looked up this matter, especially the discussions on Driver's and other papers bearing on therapy with a gold compound. It was the consensus that it is rather risky to give a gold preparation in cases of acute disseminated involvement, and one writer went so far as to say that it is practically signing the patient's death certificate to give a gold compound in such an instance.

XERODERMA PIGMENTOSUM. Presented by DR. MORRIS MARKOWITZ.

This girl, aged 3, presents brownish pigmentation covering the face, neck and upper extremities. The process began two years ago. There is marked photophobia. Ophthalmologic examination showed pigmentation of the conjunctivae and corneas but no retinal changes.

DISCUSSION

DR. DONALD M. PILLSBURY: I wonder if it would be worth while to try the application of one of the various preparations for protecting the skin from the effects of light; most of these preparations contain a quinine salt or titanium oxide, I believe.

ALOPECIA ATROPHICANS (PSEUDOPELADE) PRECEDED BY LICHEN SPINULOSUS. Presented by DR. DONALD M. PILLSBURY.

This woman, aged 48, was first seen on Aug. 30, 1933, at which time she presented a noninflammatory, grouped folliculopapular eruption distributed on the ulnar surface of both forearms, the sides of the neck, the abdomen, the lower portion of the back and the flexor surfaces of the thighs. These lesions disappeared within two months with the application of an ointment of salicylated zinc oxide. During the summer of 1934 the patient noted an increased loss of hair, and on examination in July 1934 she presented a beginning patchy alopecia in the region of both mastoids. She states that her grandmother had alopecia. The patient is a rather thin, middle-aged woman apparently in good general health. Extending from the region of both mastoid processes are patches of alopecia with moderate cicatrization. There is no erythema. The hairs at the margins of the patches are easily removed and show a marked gaping of the follicular orifices. There is a fairly marked glassy sheath on removal of the hair. Over the vertex of the scalp the hair was diffusely thin. The serologic tests of the blood were negative. The blood count revealed: hemoglobin, 79 per cent; red cells, 4,230,000; white cells, 6,800. The results of the differential count were: polymorphonuclears, 74 per cent; small lymphocytes, 17 per cent; large lymphocytes, 5 per cent; transitional forms, 4 per cent, and eosinophils, 0. No biopsy was done. Vigorous treatment with ultraviolet rays from a quartz mercury vapor glow lamp and 1 per cent dihydroxyanthranol ointment did not produce any improvement. There was no response to therapy with small doses of thyroid.

DISCUSSION

DR. DONALD M. PILLSBURY: I should appreciate any therapeutic suggestions, although I do not think that anything can be done. I wish to point out the frequency with which pseudopelade and folliculitis decalvans are associated with other dermatoses, particularly lichen planus, keratosis pilaris, scleroderma and lichen spinulosus. In the cases that Senear described the lichen spinulosus followed the development of folliculitis decalvans.

LUPUS VULGARIS. Presented by DR. CARROLL S. WRIGHT.

This man, aged 43, has had since childhood a slowly growing inflammatory patch on the outer aspect of the right leg just below the knee. It was treated with roentgen rays, which left a scar anteriorly. On the anterolateral aspect of the upper third of the right leg he has a patch roughly 2½ by 4 inches (6.3 by 10 cm.). The upper and lateral borders present numerous nodules from the size of a pinhead to that of a pea, having an apple jelly color on examination with the diascope. The inner border is atrophic and smooth; the center is virtually clear of active papules. A Gerson-Herrmannsdorfer diet plus local application of mild roentgen therapy and trichloracetic acid has resulted in healing of the ulcerated areas and in marked improvement.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I agree with the diagnosis but not altogether with the treatment. I think that in cases of this nature one type of treatment should be tried instead of a conglomeration. A woman with lupus vulgaris under my care could not stand any caustic type of treatment. She was given a salt-free diet with high vitamin content and high fat content, and the condition cleared up. I think that diet alone should be tried in this case.

DR. V. C. GARNER: It seems to me that when there is a solitary patch of lupus vulgaris it should be subjected to excision and plastic surgery.

DR. THOMAS BUTTERWORTH, Reading, Pa.: A patient of mine with tuberculous elephantiasis of the leg has been in New York and has had innumerable biopsies; the diagnosis has always been tuberculosis. She had lesions over practically 50 per cent of the surface of the leg. Several months ago all the lesions beneath the knee were curetted and electrocoagulated and then rubbed with powdered potassium permanganate, and in a month's time there was a clean scar. Later half of the lesions of the thigh were removed, and they healed even more rapidly; just this week the rest of the lesions were treated. The next step is to build up the patient's strength and then have the surgeons attempt to anastomose the superficial lymphatics with the deep lymphatics in the hope of restoring the contour of the leg.

MILROY'S DISEASE WITH ONYCHAUXIS AND ONYCHOGRYPHOSIS. Presented by DR. J. V. KLAUDER.

This girl, aged 12, has had deformed nails since birth. She is in the seventh grade at school and is mentally alert and cooperative. She states that every two months the discolored, thickened portions of the nails of the fingers and toes fall off, a new nail appearing from underneath the involved portion and in turn falling off. For the last six months the left leg has been enlarged to the knee and has exhibited pitting edema. The patient's height, weight and stature are normal. There is a difference in the size of the right and left legs, the right being 10½ inches (26.67 cm.) in circumference, and the left, 12 inches (30.48 cm.). The distal two thirds of the nails of the fingers and toes are convex and discolored and there is an associated deformity of the big toes. There are no nevi on the body, and the hair and skin are normal. The medical examination gave essentially negative results.

DISCUSSION

DR. DONALD M. PILLSBURY: Milroy's disease is hereditary edema of the legs. I do not know whether this child's family history has been investigated, but I think that before that diagnosis can be accepted there must be records of other blood relatives suffering with the disease. It must be hereditary, at least according to Milroy's original description, and the edema is usually noted in early infancy.

DR. V. C. GARNER: I think that Dr. Klauder sounded the right note on one occasion when he said that everything has to have a beginning. This patient may be the beginning of a line of descendants with the disease.

DR. THOMAS BUTTERWORTH, Reading, Pa.: Is there any record of what the patient has been eating? The condition may be edema due to inanition.

XANTHOMATOSIS (THE SCHÜLLER-CHRISTIAN SYNDROME). Presented by DR. B. L. KAHN for DR. S. S. GREENBAUM.

This girl aged 15, is emaciated and has had "warts" off and on for about eight years. They last from eight to nine months and then disappear spontaneously for three or four weeks. Finally, after the patient suffered an attack of "indigestion" (constipation and abdominal pain) they reappeared on the back and extremities and have remained permanently. No relative has similar lesions. One year before the patient came under observation she had severe bilateral earache with a discharge from the ears for five weeks. There has been a transient jaundice (questionable) for about six months.

Physical examination revealed the following abnormalities: There was a blowing apical systolic murmur transmitted to the axilla. The right rectus muscle was spastic. The skin over both upper and lower extremities showed numerous scattered yellow papules from 2 to 4 mm. in diameter on a slightly reddened base. On the arms they occurred chiefly below the elbow, and on the lower extremities they were present chiefly on the inner surface of the thighs. There was practically no panniculus adiposus. The specific gravity of the urine ranged between 1.014 and 1.040. Dextrose was present consistently, ranging from 0.65 to 4 per cent. On two occasions there was a faint trace of acetone. The number of white blood cells varied from occasional to as high as 20 cells per field; that of red cells varied from 3 to 5. Occasionally there were a few hyaline epithelial and finely granular casts. The blood sugar ranged from 139 mg. per hundred cubic centimeters on admission to as high as 185 mg. On Jan. 14, 1935, the carbon dioxide content of the blood was 60 volumes per cent. A test for dextrose tolerance on Dec. 4, 1934, gave the following results: The blood sugar content was 150 mg. per hundred cubic centimeters before intake; 178 mg. one-half hour after; 234 mg. one hour after; 220 mg. two hours after, and 157 mg. three hours after intake. On December 5 the test gave essentially the same results, but the figures were slightly higher. On December 5 the Schilling index showed: myelocytes, 0; metamyelocytes, 0; stab cells, 5 per cent; segmented forms, 60 per cent; lymphocytes, 32 per cent; monocytes, 2 per cent. The bleeding time was three minutes; the coagulation time, five minutes and four seconds. The icterus index was from 6 to 8. There were 4.9 per cent reticulocytes. Serologic tests were negative. The chemical examination of the blood showed: calcium, 11 mg. per hundred cubic centimeters of blood; urea nitrogen, 22 mg.; phosphorus, 4.38 mg.; chlorides, 557 mg.; cholesterol, 226 mg.; uric acid, 3.86 mg.; creatinine, 1.02 mg.; total blood protein, 7.61 Gm.; serum albumin, 5.21 Gm., and serum globulin, 2.4 Gm. The blood count on Nov. 21, 1934, showed: hemoglobin, 80 per cent; red cells, 4,380,000; white cells, 8,000; polymorphonuclears, 63 per cent; large monocytes, 31 per cent; transitional forms, 1 per cent. The bile culture showed Bacillus coli and Bacillus alcaligenes. On Jan. 2, 1935, the cholesterol content rose to 453 mg. per hundred cubic centimeters of blood despite the fact that the patient was following a fat-free diet, and at that time the calcium content was 8.6 mg., and the phosphorus content, 4.2 mg. The basal metabolic rate on Nov. 24, 1934, was +11; on November 27 it was —8, and on Jan. 12, 1935, +25.

A roentgenogram of the skull on November 22 showed several clarified areas with a moth-eaten appearance in the posterior portion on the right side but disclosed no other abnormalities. The pituitary fossa was normal. Roentgen examination of the long bones showed moderate decalcification with several scattered areas of destruction in the left ulna and the right tibia and evidence of an old fracture of both bones of the right forearm. The lower end of the femur showed broadening of the bone with a thinning of the cortex and coarse bony trabeculation. This change has been described as having the appearance of an Erlenmeyer flask and is pathognomonic of Gaucher's disease. The lesions in the skull were like those usually found in patients with xanthomatosis. The diagnosis, from the roentgen evidence, especially from the appearance of the femur, was Gaucher's disease.

A roentgenogram of the abdomen on November 22 showed the kidneys to be normal in size and position and to contain no calculi. The lumbar portion of the spine was normal.

Cholecystography on November 28 showed a gallbladder normal in size, shape and position; it concentrated the dye normally but after a meal with high fat content showed impairment of contraction, indicating impairment of function. There was no evidence of calculi.

On December 13 the bones of the carpus, hands and lower ends of the radius and ulna were found to be markedly decalcified and to show rather coarse bony trabeculation. The jaws were normal; the mastoids, sclerotic. The eyegrounds appeared normal. On December 3 biopsy on a cutaneous lesion showed cholesterol and neutral fat, but no Gaucher cells were seen. The patient was put on a fat-free diet and insulin therapy on Nov. 7, 1934, and on Jan. 17, 1935, she received roentgen therapy to the pituitary gland.

This patient is presented to bring out the following points: (1) persistent hyperglycemia; (2) disappearance (almost complete) of the cutaneous xanthomas with insulin therapy, despite a persisting hyperglycemia and (3) increase in blood cholesterol with a fat-free diet.

DISCUSSION

Dr. D. M. Sidlick: I believe that the fact has been established that the local manifestations do not depend on hyperglycemia. The patient may have hyperglycemia treated with insulin, the general condition improving but not influencing the dermatologic manifestation, and I presume that this is the situation in this case. Then again there are cases in which only small quantities of insulin have considerably influenced the local manifestations. It is obvious, then, that while there is an etiologic relation between hyperglycemia and the local manifestation, there is little relation so far as therapy is concerned.

Dr. S. S. Greenbaum: The lesions are not inflammatory. They are not of the type which occur in xanthoma diabeticorum.

Dr. F. D. Weidman: I think that this patient's condition corresponds to that which existed in cases which Dr. Freeman and I reported. At autopsy our patients showed extensive xanthic erosions of the calvarium, marked cirrhosis of the liver and invasion of the pituitary and pineal glands by xanthomas. In cases of xanthomas occurring in young patients attention should be paid to the base of the brain also when roentgenograms are made. In a patient whom Dr. Greenbaum observed for a long while there was no disease in the pituitary gland, but there was a marble-sized granuloma of the pons. While such a lesion is scarcely to be regarded as being situated within the cranium and being definitely related to the pituitary, still it is in the general region of highly important nerve centers which may have to do with general metabolism. Witness the Séquard picture of the floor of the fourth ventricle. This patient has a tremendously high palatal roof. There may be some congenital vice in the configuration of the bones which is interfering with the development of the pituitary gland. Roentgenograms of the base of the brain should not be omitted in the further working up of the case.

NEW YORK DERMATOLOGICAL SOCIETY

FRED WISE, M.D., *President*

Jan. 22, 1935

R. H. RULISON, M.D., *Secretary*

EPITHELIOMA OF THE LOWER EYELID: RESULTS OF TREATMENT. Presented by DR. PAUL E. BECHET.

B. M., a woman aged 62, fourteen years ago noticed a growth on the lower left eyelid which slowly increased both in size and extent. By March 7, 1930, when she first came under observation, the entire lid was covered by a typical epitheliomatous growth, which had already destroyed a considerable part of the lid. The lid was drawn down as much as possible with adhesive tape, and 2½ skin units (187 roentgens) of unfiltered rays was administered through an aperture in a lead shield. The shield covered only part of the eyeball, the lower third of the eyeball being exposed to the rays. Because of fear of causing severe conjunctivitis with possible resulting ulceration, no shield was placed over the eyeball. About two months later, on May 13, 2½ units of roentgen rays was again given. Four month later the same dose was repeated, so that in a period of six months the patient received 7½ skin units (562 roentgens) unfiltered and with the lower third of the eyeball unprotected.

Excellent results followed the treatment. The lesion has remained entirely well for four years, the eye remaining unaffected, and the cosmetic results speak for themselves. The patient is presented because of the fact that irradiation consisting of a total of 7½ skin units, in three doses of 2½ units each, administered over a period of six months, apparently has had no deleterious effect on an eye the lower third of which had been left unshielded.

DISCUSSION

DR. HOWARD FOX: The possibility of producing a cataract after exposing the eyeball to roentgen rays has recently occurred to me. It is encouraging to see that in this patient no damage has appeared at the end of five years. The time in which damage may occur has not yet expired, I think, and I should like to know the result at the end of ten or even twenty years.

DR. JOSEPH J. ELLER: I came a few minutes late and did not see this patient, but I have watched the progress of various patients with epithelioma of the lower eyelid since I have been in practice, and in the last few years I have come to the conclusion that the best method of treatment is excision by the scalpel followed by repair by plastic surgery.

DR. FRED WISE: This patient was presented chiefly to demonstrate that 7 skin units of roentgen rays unfiltered can be given to the eyelid in divided doses without protection to the eyeball and that after five years the eyeball has not suffered any ill effects. What is Dr. Eller's opinion about that?

DR. JOSEPH J. ELLER: I share Dr. Fox' opinion about roentgen therapy. I should be a little apprehensive about its consequences in this case, even though five years have elapsed since the treatment was given.

DR. EUGENE F. TRAUB: I did not see the patient either, but the answer to the question of the possible development of a cataract depends entirely on whether or not the cornea received any direct radiation at the time the treatment was administered. I mean that it is possible, in fact customary, to administer the rays at such an angle that the eyeball itself may be completely screened with lead. I generally treat all lesions on the eyelids with some form of radiation, possibly first combined with endothermy, but the trick is to keep the rays from striking in a line with the eyeball. It is usually not necessary to cover the eyeball with a

protective disk, as in most instances the lesion can be drawn out of the range of rays which would be dangerous to the eye. If that was done in this case, of course there will not be any danger that a cataract will result. If not, of course, only time will tell.

DR. FRANK C. COMBES: I agree with what Dr. Traub has said.

DR. HOWARD FOX: The question under discussion is not how to avoid exposing the eyeball to rays but rather whether the roentgen rays when applied to the eyeball can produce a cataract. Although a massive dose was administered to this patient, it is pertinent, I think, to discuss the possible ill effects of fractional doses of roentgen rays. I have given such treatment in a number of cases of eczema of the eyelids without inserting a metallic disk beneath the lids. While the insertion of the disk is not difficult, even when the eye is anesthetized it is disagreeable to some patients and rather terrifying to others. To some it suggests that irradiation of the eyelids has an inherent danger. Personally I have never known a cataract to follow a series of fractional doses and should like to hear expressions of opinion and experience of others present.

DR. E. B. TAUBER, Cincinnati (by invitation): I think there are two factors to be thought of in dealing with this subject. One is that the occurrence of cataract after exposure to roentgen rays is usually in a person in whom possibly a cataract would have appeared anyhow at the age at which cataract usually develops, and, of course, cause and effect are brought into play and dwelt on in such cases, and the development of the cataract is attributed to irradiation. The second factor is that irradiation in larger dosages is not decidedly injurious. Hence, I do not think that there is as much reason to fear ill effects as many careful men seem to think, and I believe that if the reported cases of cataract after exposure could be statistically studied the injuries would be found to be bilateral rather than unilateral in a large proportion of cases.

DR. EDWARD R. MALONEY: I agree with what Dr. Fox has said. In spite of the fact that the patient has had no trouble yet, I should like to see the results in from three to five years more. However, it seems to me that in all probability the eyeball was somewhat protected. Dr. Bechet said that he cut a hole in the shield to irradiate the affected area; hence it is quite possible that the eyeball was protected. I think it is a dangerous thing to do, however, and in spite of the fact that the patient has no trouble now, ill effects may appear a few years from now.

DR. FRED WISE: Although I never insert the guard over the eyeball myself, at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital the following procedure is used: Cocaine is instilled into the eye, and the guard is coated with sterile oil and slipped under the lids. When it is removed the patient has no trouble whatever. Therefore, I think a guard should be used whenever roentgen treatment is applied to the eyelids and the lesion overlies the eyeball.

DR. PAUL E. BECHET: The reason I did not use the guard was that an ophthalmologist told me that he had observed some serious ulcerations of the eye after a guard had been used on a patient who had received roentgen irradiation for some condition of the eyelid. That worried me a good deal, and I decided not to use the guard. In all three exposures, as may be noted in the history, I pulled down the eyelid with adhesive tape, as Dr. Traub has suggested, but I found difficulty in doing so because of the extensive distribution of the epithelioma. Of course, only the lower third of the eyeball was exposed because the patient had a lead shield over the face and the adhesive tape pulled the lid down to some extent. It was difficult to pull the lid down altogether because the epithelioma was on the inner side of the lid. My aim in presenting this patient was to stimulate discussion as to the danger of glaucoma's developing later if the eyeball is not covered and the danger of the guard's causing ulcerations with possible loss of sight or serious ocular trouble. It is five years since this patient has had her last roentgen treatment, and I have had an ophtholmologist examine her. He tells he that her eye is in perfect condition. She has not had to change her glasses.

Dr. Charles Mallory Williams: Has any one here any statistics showing the amount of injury to the eye after exposure to roentgen rays? If not, the discussion is entirely academic.

Dr. A. Benson Cannon: I received a letter from an ophthalmologist today about a patient whom I have treated for eczema and for an extensive burn of the face caused by roentgen rays. He asked, since that patient has an incipient cataract in each eye, whether I thought there might be any connection between the patient's eczema or the burn and the cataracts. I think that Dr. Fox' question is interesting, and I, too, should like to know whether the roentgen rays or the eczema could have caused my patient's cataracts. She has noticeable changes in the skin over her face, neck and chin due to the radiation as well as to the eczema.

Dr. Fred Wise: In reply to Dr. Fox' specific question, I wish to state that I have never seen any ill results from irradiating the entire face, including the eyelids, with fractional doses of roentgen rays, but I have given only enough fractional doses at weekly intervals to avoid defluvium of cilia, that is, about three quarters of a unit. I have never given enough roentgen rays to the eyelids to cause loss of cilia in routine therapy.

Dr. Howard Fox: In giving enough roentgen rays to cause epilation of the eyelashes I have always used a thin band of lead to protect the lashes.

Angioma of the Penis. Presented by Dr. Edward R. Maloney.

J. T., a youth aged 18, born in Russia, presents on both sides and on the lower aspect of the glans penis a soft, bluish tumor which has been present since the patient was 8 years old. This patient is shown because of the unusual location of the angioma.

DISCUSSION

Dr. Howard Fox: The appearance of the lesion suggests a tortuous mass of varicose veins, a condition that I do not recall having seen in this locality. As to treatment, I suggest injections of some sclerosing fluid, such as that used in the treatment of varicose veins of the leg.

Dr. Charles Mallory Williams: The lesion is too old to be subjected to treatment with radium. If radium had been used when it first appeared there would have been a good chance for cure.

Dr. Joseph J. Eller: I agree with Dr. Williams. This lesion would be highly resistant to radium or roentgen therapy now. I suggest that it be left untreated.

Dr. Edward R. Maloney: I showed this patient merely because of the unusual location of the lesion. I had never seen one at that site, and, as Dr. Fox said, it does look like a bunch of varicose veins. I called it angioma to be on the safe side. I agree with the idea of treatment by injection.

Dr. Fred Wise: I disagree with Dr. Eller about the desirability of leaving this lesion untreated. I think that because of its location it should be treated and an attempt should be made to remove it.

Multiple Concentric Pigmented Nevi. Presented by Dr. Frank C. Combes.

F. M., a boy aged 16, presents on the chest a flat, brown nevus about 4 mm. in diameter. Surrounding the lesion is an even area of normal skin about 2 mm. in diameter, limited by a perfect pigmented circle about 2 mm. in width. There are also three similar lesions on the back. These lesions have developed within the last two years. In addition, the patient has numerous pigmented nevi.

DISCUSSION

Dr. Charles Mallory Williams: This case is interesting. The occurrence of so many nevi is not unusual, but the occurrence of the unusual dot in the middle is distinctly rare. I do not think I ever saw a lesion like that before. As a curiosity it is interesting.

Dr. Eugene F. Traub: I agree with Dr. Williams. I have seen at least one other patient at the hospital with an eruption of exactly similar arrangement. No logical explanation was found.

Dr. Fred Wise: Is this not similar to Sutton's leukoderma acquisitum centrifugum as far as the pigmentary part of the lesion is concerned?

Sarcoid? Presented by Dr. Eugene F. Traub.

J. O'R., a man aged 62, born in the United States, presents a nodular eruption on the forehead near the hairline and a single large lesion on the back. The lesion on the back appeared about six years ago and increased steadily in size. The lesions on the forehead have been present for several years, but have not increased materially in size, remaining more or less stationary after a slight initial growth. The patient states that one small nodular mass on his back has disappeared spontaneously.

The nodules on the forehead are near the hair margin and measure from about 1 to 3 cm. in diameter. They are slightly elevated, show a marked infiltration in the deep portion of the cutis and are light pink. At times they are almost inconspicuous. The mass on the back, on the other hand, presents a striking appearance. This lesion is about 3½ or 4 inches (8.8 or 10 cm.) in diameter, is raised above the skin from 1 to 3 cm. and is deep reddish purple. There seems to be a marked engorgement of the superficial vessels which is responsible for the color. The mass itself consists of a large lobulated tumor, the individual parts of which vary slightly in consistency, presenting from a doughy to a rather firm, almost cartilaginous sensation on palpation. The growth on the back seems rather invasive and gives the impression that there may be considerable infiltration of the skin beyond the distinctly palpable borders of the mass. The Wassermann reaction was negative.

A biopsy was performed and reported on as follows: The section shows islands of dense cellular exudate in the midcorium. These are not surrounded by any inflammatory zones. The cellular exudate consists of lymphocytes, connective tissue cells and pale-staining cells. The epidermis is normal. The zone of connective tissue fibers between the cellular exudate and the epidermis does not show any inflammatory reaction. The diagnosis is sarcoid(?).

DISCUSSION

Dr. J. Frank Fraser: Examination of the section certainly suggests the diagnosis of sarcoid. The distribution is in the upper portion of the corium, and for that reason I think that it can be classified as belonging to Boeck's variety. Clinically the eruption does not look like sarcoid. It looks more like an angioma or like the so-called angiosarcoma.

Dr. Howard Fox: Does the section show any evidence of lymphoblastoma?

Dr. J. Frank Fraser: I do not believe so. It does not look like lymphoblastoma histologically, and the section I examined does not show any neoplastic features.

Dr. Charles Mallory Williams: In Ewing's book there is a description of a perithelioma, which is a tumor frequently involving skin and connective tissues. That description fits fairly well with the clinical appearance of this patient's lesions. The lesions often last for years before showing malignant changes. They are large, arise from blood vessels and often show greatly dilated vessels, thus assuming an angiomatous appearance. I offer this simply as a suggestion.

Dr. J. Frank Fraser: MacCallum does not accept the term perithelioma, as there is no such tissue as perithelium. Further histologic study of other sections should be carried out. The lesions may be angiosarcoma.

Dr. Howard Fox: I am getting to the point at which I believe that almost any type of eruption can be a sarcoid. There is certainly a great difference

between the few macules of Dr. Combe's patient and the large mass presented by this patient, regarding which I should not have even thought of sarcoid as a diagnosis. Is this lesion radiosensitive?

DR. E. B. TAUBER, Cincinnati (by invitation): I feel a great deal as Dr. Fox does. I am beginning to believe that anything can be sarcoid, but clinically this patient's eruption does not appear to me like Boeck's sarcoid. However, Dr. Fraser says that is the niche into which this condition fits. Clinically, it looks to me like a sarcoid of the Darier-Roussy type, but I have never seen one of this size. I am absolutely at a loss as to how to classify the disorder; I think that the diagnosis will have to be left to the pathologist and that for the present the growth may be regarded as a Boeck sarcoid or a sarcoma-like lesion.

DR. EUGENE F. TRAUB: May I ask the members for a few suggestions as to therapy?

DR. A. BENSON CANNON: I cannot reconcile the histologic report with the clinical picture. I have never seen a sarcoid as large as the tumor this patient presents on the back, nor have I ever noticed in a sarcoid the bluish, angiomatous color and the multiple nodules that compose about one half of this tumor. Moreover, there is the unusual appearance presented by the small radiating blood vessels of the outer side of the tumor, while the inner and upper parts of the tumor are composed of nodules that reach upward toward the cervical region of the spine as though following the course of the lymphatics. About 3 inches (7.5 cm.) above this area is a discrete hazelnut-sized nodule which, though chiefly subcutaneous, involves the skin also. I suggest wide incision of the entire tumor; numerous sections from various parts of the growth should be made and studied. I believe that a thorough physical examination of the patient, roentgenograms of the chest and an examination of the blood should all be made before the diagnosis of lymphoblastoma is ruled out. I think that the lesions more nearly conform to the picture of sarcoma than to that of any other members of that group.

DR. FRANK C. COMBES: I agree with what Dr. Cannon and with what Dr. Fraser said. The lesion clinically does not look much like sarcoid to me. Some day soon it will become evident that there are a large group of conditions which have been carelessly called sarcoid much as Kaposi used the term to include a series of unrelated dermatoses. I do not think that it is possible to make a diagnosis of sarcoid merely from a histologic section. There are too many other conditions which simulate sarcoid. Before a diagnosis of sarcoid is made, the eruption should be considered as a tuberculid and investigation should be made regarding the possibility of tuberculous etiology, graded tuberculin tests and examination of the lungs for old infiltrations and peribronchial nodes. Otherwise, the only statement one can make is that the patient has a sarcoid-like lesion, possibly a lymphoblastoma.

DR. PAUL E. BECHET: Dr. Cannon has expressed exactly my views of the case. Despite the deep respect I have for Dr. Fraser's opinion on histologic observations, I must say that clinically the color of the lesion, its excessive hardness and the presence of nodules and even satellite nodules certainly do not coincide with the description of any type of sarcoid. I should want to eliminate the possibility of some slowly growing sarcoma before making a diagnosis of sarcoid.

DR. FRED WISE: I agree especially with the opinions expressed by Dr. Cannon and Dr. Bechet. I appreciate the significance of the histologic examination as much as any one, but I cannot reconcile myself to classifying this lesion as a benign growth like ordinary sarcoid. I believe that the patient has a form of lymphoblastoma or what has been called the Spiegler-Fendt type of sarcoma. An article on this subject by Lewis appeared in the January issue of the ARCHIVES (Lewis, George M.: Is Spiegler-Fendt Sarcoid a Clinical or Histologic Entity? ARCH. DERMAT. & SYPH. **31**:67 [Jan.] 1935). I suggest, in addition to what Dr. Combes said, that repeated examinations of the blood and of the bones of the hands and feet be made to see if the patient has any cystic changes in the skeletal system.

DR. EUGENE F. TRAUB: I have had little opportunity to study this patient, as he has been seen only once before presentation. Thus far only a Wassermann test and a biopsy have been performed. One thing which most of the members did not discuss is the fact that he has a single or possibly even a group of small separated nodules on the forehead. Nor was any mention made of the fact that there is a history that another small lesion on the back disappeared spontaneously. When I saw this patient for the first time it was my opinion that the lesion was either a lymphoblastoma, possibly of the mycosis fungoides type, or a sarcoma, and with this thought in mind I gave the patient a rather unfavorable prognosis. A section was removed for diagnostic purposes, and it was intended that he should return to have the entire lesion removed if that was deemed necessary. I was somewhat surprised at the report of sarcoid, but in the section which was removed there were no histologic features suggestive of lymphoblastoma. The patient received no treatment before I saw him, and there has been no opportunity to try irradiation to see whether there would be any favorable response. Most of the members probably remember that patient whom I presented at a meeting of the New York Academy of Medicine about six months ago. The patient, an Italian, had a large lesion on the temple and several isolated lesions on the scalp. The diagnosis made from a section was that of sarcoid, but the late Dr. Highman disagreed and said that microscopically and clinically the lesion was a sarcoma. Comparativey small doses of roentgen rays caused the lesion almost to disappear. Subsequently it returned, and many metastatic lesions developed over the entire body. This caused differences of opinion as to the diagnosis. Several lesions were removed, and it could not be definitely settled even on a microscopic basis whether these nodular masses represented lymphoblastoma (mycosis fungoides) or sarcoma. The disease progressed so rapidly that when the patient was notified to come into the hospital he was already bedridden, and he may have died of the disease. Mindful of that occurrence, I wanted to give this patient every opportunity to receive the best advice possible before instituting any radical form of treatment. In view of the expressed opinions I shall attempt to remove the lesion as widely and as thoroughly as possible and get a further report on the tissue removed.

ACRODERMATITIS CONTINUA OF HALLOPEAU. Presented by DR. EUGENE F. TRAUB.

S. N., a man, aged 23, born in the United States of Hungarian parentage, was presented at a meeting of the New York Dermatological Society in October 1929 (ARCH. DERMAT. & SYPH. **21**:510 [March] 1930). Since that presentation a considerable amount of laboratory work has been done. Chemical examinations of the blood have been repeatedly negative. The Wassermann reaction has been negative on at least three occasions. The spinal fluid is normal. Examinations of the urine have given the following results: On March 5, 1929, the reaction was acid; the specific gravity was 1.025; there was no albumin, sugar or indican; there were a few epithelial cells; the phenolsulphonphthalein test showed an abundance of the test substance, and mucus and pus cells were present. On March 30 the reaction was acid; there was no albumin or sugar; red blood cells, white blood cells and pus cells were found. On August 24 the reaction was acid; the specific gravity, 1.022; there was no albumin, sugar or indican; a few epithelial cells and much pus were found.

In addition to the laboratory examinations the patient has also been subjected to thorough investigations for focal infections, and several infected teeth have been extracted. The neurologic examination gave negative results. He received more than fifteen injections of arsphenamine and a great variety of local treatment, none of which had any material effect in arresting the process.

Since he was presented in 1929 the eruption has spread to the forearms and trunk, at which sites he presents patches of an erythematosquamous appearance, though in some areas there is a suggestion that there may have been some pustules which are now crusted. Only in the past year or two has an eruption appeared elswhere than on the hands and feet.

DISCUSSION

DR. E. B. TAUBER, Cincinnati (by invitation): In Buffalo I had the opportunity of seeing patients with a condition similar to that of this young man. Dermatologists practically attributed the entire condition to an infection with Monilia. I am not sure that that diagnosis is correct. I believe that Monilia is a contamination which has persisted for a length of time. Some one mentioned the question of psoriasis. I cannot quite agree. Clinically the disorder has many characteristics of psoriasis, such as the dryness and scaling, but I have never seen psoriasis which persisted for twenty-three years without showing some regression, without, in fact, being at some time perfectly healed. I do not believe that this has occurred in this patient's case. My colleagues and I have had two patients in whom the condition was similar to that of this patient, but we had never thought of an infection with Monilia. When I returned to Cincinnati from the meeting in Buffalo I examined both patients and found Monilia in both. The only method of treatment with which we had any success was the old remedy consisting of a 33.3 per cent acid solution of mercuric nitrate diluted 1: 10 and used in packs. With this, an almost complete regression took place, but a recurrence appeared in a few months. I think that the diagnosis which Dr. Traub made, acrodermatitis continua of Hallopeau, is the correct one.

DR. A. BENSON CANNON: I think that Dr. Traub's diagnosis is good, but I believe that psoriasis should be considered as well, and probably if I had to make a definite diagnosis I should choose that of psoriasis rather than that of acrodermatitis of Hallopeau. I think that the sharply circumscribed, slightly raised, red plaques limited to the palms and fingers and finger-nails and the intense dryness of the skin with silver-colored dry scales in layers to which attention has been called give more nearly a picture of psoriasis. The lesions on the arms are, I believe, more nearly like those seen in that disease. A few years ago I saw a patient with a somewhat similar condition who was also examined by Dr. Barber of London. In that case the diagnoses considered were dermatitis of Hallopeau, psoriasis or an infection with Monilia. The lesions on the palms were strikingly like those of this patient, though the secondary lesions observed on the forearms and dorsa of the feet were more like those caused by fungus infections.

DR. FRANK C. COMBES: I incline toward the diagnosis of psoriasis in spite of the fact that the condition has remained so constant and has shown no remissions for such a long time. It was always my impression that Hallopeau's disease did not produce the micaceous scaling which suggests psoriasis. As regards treatment, I suggest that ointment of mercuric nitrate be used. I have used it with seemingly good results in some cases. I use a concentration of from 3 to 5 per cent, as the official 10 per cent ointment is too strong.

DR. PAUL E. BECHET: I agree with Dr. Tauber. The diagnosis of psoriasis did not occur to me. The scales are too large. There are fissures between them as though the lesions had been moist at one time. It seems to me that the scales are due to drying of the moisture. As far as the question of Monilia is concerned, I recently had a patient at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital who had Monilia in the stools and on the hands and wherever lesions appeared. Whether that has anything to do with the condition, I do not know. A diagnosis of Hallopeau's disease was made. It is interesting, however, that Dr. Tauber should have had two patients who also showed Monilia. I think that this patient has Hallopeau's disease and not psoriasis.

DR. CHARLES MALLORY WILLIAMS: I agree with Dr. Tauber. I think that this patient has a typical case of Hallopeau's disease. There are many points in favor of that diagnosis. The disease begins along the finger-nails, involves both hands and one foot, spreads centripetally and in the course of its progress destroys the finger-nails. This patient's nails are thin or absent and do not look like those of patients with psoriasis. The disorder advances by a sharp border, and pustules are found on the periphery as well as throughout the lesions. The lesions are nearly always small, and pustules are not apparently an essential feature. They

are not always present. I remember one patient whom I followed for many months: Sometimes there were groups of pustules, and at other times there were none. The disease is essentially a dry, red, scaly, inflammatory condition going on to atrophy. The fingers, as in this patient, are almost as much atrophied as those of patients with scleroderma. That is not true in cases of psoriasis. I cannot imagine psoriasis lasting as long as this patient's disorder has without showing periods of regression. If the disease were psoriasis there would not be scales pointing in such as this patient has. They would rather point out. In this patient the disease is advancing under the skin. I think that the presence of Monilia is purely accidental. Any one who spends many hours examining nails and interdigital spaces for Trichophyton and makes cultures will be much surprised at the enormous numbers of infections with Monilia and at the small number of infections with Trichophyton he discovers. Monilia is a common contaminant. In a patient who was followed for months at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital no organisms were ever found on culture. Many different mediums were tried. In that patient the condition was much worse than in this one. It involved both hands and both feet, and the patient was absolutely crippled by it. I think dermatologists are too much inclined to ascribe diseases to any fungus or organism that they happen to find on the surface of the lesion.

Dr. Howard Fox: I agree with Dr. Williams that in all probability the infection with Monilia is merely secondary and is not the cause of the disease. The diagnosis certainly is either Hallopeau's disease or psoriasis. The patches on the arms have micaceous scales, and I am inclined to regard the entire process as psoriatic.

Dr. Edward R. Maloney: I agree with those who think that the disorder is psoriasis. It seems to me that the picture fits in well with that of pustular psoriasis as seen in patients who have been presented lately. The more recent lesions, particularly those on the upper part of the arm, impress me as those of psoriasis and not as those of Hallopeau's disease. It seems to me that it would be a good idea for Dr. Traub to make a biopsy.

Dr. Fred Wise: I am not unmindful of what has been said about psoriasis, but if ever I saw an eruption which corresponds to the picture of Hallopeau's disease in every minor and essential detail, this patient's does, as Dr. Williams has pointed out. As to Dr. Traub's request for suggestions relating to treatment, I advise a simple treatment which carries but little risk of setting up a dermatitis. It consists of the persistent use of a 2 per cent aqueous solution of gentian violet over a period of two months. As to the treatment Dr. Combes suggested, I have had no experience with it, but I have had a rather favorable experience in the treatment of two patients with gentian violet.

Dr. E. B. Tauber, Cincinnati (by invitation): In all these cases I like to add 1 per cent acriflavine hydrochloride to the gentian violet, as in that way there is a therapeutic action on all organisms, both gram-positive and gram-negative, which is desirable, since in many long-standing lesions there may be a mixed infection.

Dr. A. Benson Cannon: I wish to ask a question concerning the significance of finding Monilia in the cutaneous lesions and in the stools. Of course, it is known that Monilia in the stool is often nonpathogenic, but if a patient gives a decidedly positive reaction to an extract of Monilia cultured from the stool, would that not at least suggest that the accompanying dermatitis may be caused by that fungus?

Dr. Charles Mallory Williams: I do not wish to be understood as saying that Monilia is not the cause of a dermatitis. It is the cause of a great many dermatoses, but the occasional finding of that fungus in a pustule is not evidence that it is the cause of the dermatitis.

Dr. A. Benson Cannon: Should a patient give a strongly positive cutaneous reaction to an intracutaneous injection of an extract made from Monilia cultured

from the skin or stool, would not the reaction indicate that the patient might be suffering from an infection with Monilia?

Dr. Fred Wise: The finding of Monilia in the skin in cases of this kind seems to have little significance in relation to the etiology of the dermatosis.

Dr. Charles Mallory Williams: I agree with what Dr. Wise has just said.

Dr. Frank C. Combes: Would it be of any help to test such a patient intracutaneously with an extract of Monilia in regard to any focal reaction in the lesion he presents? Would there be any diagnostic significance in that reacion, or would it not be specific enough if one should get a good positive local reaction and at the same time a focal reaction in the lesion?

Dr. Charles Mallory Williams: Personally I think the reaction might be significant, but I should like to see a collection of cases. I think that a long series of cases would be necessary. In a single case the reaction would not mean much, but it would be an indication.

Dr. Eugene F. Traub: This patient was first seen in about 1927, and from then until 1929 he was under close observation; for a portion of that time he was a patient at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. At that time he presented no lesions on the body, arms or legs, the only involved parts being the hands and the left foot; the condition did not even remotely suggest psoriasis, and although my co-workers and I isolated Monilia from some of the lesions this was not regarded as having any bearing on the condition. He received the usual remedies accorded a patient with acrodermatitis continua, and although improved somewhat, not a single one of the lesions on the hands or foot cleared up entirely. Since 1929 he has received only indifferent treatment in his home in New Jersey, and I now find that since I last saw him the disease has progressed on the original sites that were affected and new areas of involvement have appeared elsewhere on the extremities and on the body. Again material from some of the lesions was cultured but failed to show a growth of either Monilia or any form of bacteria. Similarly, negative results were obtained in an attempt to examine and grow material from the stools. A recent article was written by H. W. Barber entitled "Acrodermatitis Continua vel Perstans (Dermatitis Repens) and Psoriasis Pustulosa" (*Česká dermat.* [supp.] **12**:20, 1931). According to the description in this article, this patient undoubtedly presents a typical case of Hallopeau's disease, the differences between this condition and pustular psoriasis being clearly stressed. The new lesions on the upper portion of the arm and on the trunk are difficult to account for, but similar lesions have been previously described in such cases.

Dr. Charles Mallory Williams: If one of the dry lesions occurred on the palms by itself it would reproduce the picture of the dry lesion on the arm. Forget the pustule. Think of the dry lesions on the palm and on the arm. They are practically identical. The fine branny silvery scales occur regularly in this disease and are more common than the pustules.

Lichen Planus of Ten Years' Duration. Presented by Dr. Howard Fox.

P. E., an American-born watchman aged 35, has suffered from an eruption on the left wrist for ten years. One year previously a generalized, symmetrical, rather sparse eruption of typical lichen planus appeared on the extremities. This is situated on the flexor aspect of the wrists and forearms and on the legs, particularly on the ankles. It consists of flat, pinhead-sized papules, many of which show a central umbilication. Some are discrete, and others, by coalescence, form small rings or crater-like lesions. They all present a shiny and violaceous appearance. The lesion on the left wrist, which has been present for ten years, is apparently of the same type as the rest of the eruption. It is rectangular, has a clear center and is 1¼ inch (3.18 cm.) in its longest dimension. There is apparently some slight atrophy. The oral mucosa and the genitalia are not involved. The patient

complains of only slight itching, and no marks of scratching are present. The eruption has undergone considerable involution in the past five weeks under treatment with roentgen rays.

DISCUSSION

DR. HOWARD FOX: Although the eruption has undergone considerable involution in the past five weeks as a result of roentgen therapy, I think that the diagnosis can still be made with reasonable certainty. There was no question of the diagnosis five weeks ago. The point of interest is the quadrangular patch on the wrist which has been present for ten years; its general appearance is similar to that of the smaller patches.

DR. CHARLES MALLORY WILLIAMS: When I first saw this patient I thought that the patch was lichen planus, and I still think so. I think it is unusual for a patch on the upper extremity to last as long as that, but since it is known that hypertrophic lichen planus on the legs and patches of lichen planus on the tongue may be of indefinite duration, it does not seem at all impossible for a similar patch to occur on the upper extremity.

DR. FRANK C. COMBES: Since the lesions on the wrist are undergoing the same evolutionary changes as the others under treatment, all the lesions are probably lichen planus. The appearance of all suggests atrophy. I do not mean that they are all lichen planus atrophicans; they probably represent merely atrophy following lichen planus.

DR. HOWARD FOX: Dr. Williams mentions the long duration of the hypertrophic type of lichen planus and that of lichen planus confined to the mouth. The longest duration in my series of cases of involvement of the mouth was eight years. I have recently seen another patient who also had lesions of eight years' duration; he had been under the care of Dr. Carroll Wright for a long time.

REPORT ON A PATIENT PREVIOUSLY PRESENTED. DR. HOWARD FOX.

H. F., a man aged 25, was presented as possibly having mycosis fungoides at the meeting of the New York Dermatological Society on Dec. 18, 1934 (ARCH. DERMAT. & SYPH. **32**:157 [July] 1935).

Histologic examination by Dr. T. J. Riordan gave the following results: Under low magnification there were seen markedly acanthotic rete, many papillary inclusions and absence of the granular layer; there was no scale because it was probably washed off in preparation. One place showed a patch of parakeratotic scale and intercellular and intracellular edema. Diffuse infiltration of the papillary rete extended along the blood vessels of two subpapillary plexuses. Under high magnification the infiltrate was seen to consist of small and large round cells, plasma cells, eosinophils, occasional polymorphonuclear leukocytes, erythrocytes and epithelioid cells.

The specimen showed an example of a chronic inflammatory process or dermatitis. The polymorphous infiltrate and the distribution of the infiltrate pointed to mycosis fungoides.

DISCUSSION

DR. J. FRANK FRASER: I should be inclined to think that the lesion is a reticulo-endothelial tumor. That is to say, it would belong in the group of mycosis fungoides, lymphosarcoma or Hodgkin's disease. I am more inclined to favor the diagnosis of mycosis fungoides (1) on account of the distribution high up in the papillary layer and (2) on account of the polymorphism and the presence of numerous eosinophils. The lack of marked fibrosis speaks against the diagnosis of Hodgkin's disease. There is some tendency to fragmentation of the nuclei, which is also in favor of the histologic diagnosis of mycosis fungoides.

ERYTHROPLASIA. Reported by DR. HOWARD FOX.

S. C., aged 25, an American salesman, has suffered from an eruption confined to the glans penis for ten months. The lesions attained their maximum development during the first three months. The eruption consists of a diffuse patch covering the greater part of the glans penis, one small adjacent patch and two pea-sized lesions on the corona. They are all dull red, sharply marginated, slightly elevated and wrinkled, and they ooze sufficiently to cause sticking of gauze dressings. There is some itching of the shaft of the penis, but none of the lesions themselves. There are no other lesions of the skin or oral mucosa. Histologic examination previously made by Dr. Satenstein confirmed the clinical diagnosis. There was no improvement after 6 fractional (75 roentgens) unfiltered doses of roentgen rays and injections of sodium arsenate given by Dr. Morse.

DISCUSSION

DR. HOWARD FOX: This case is reported to obtain discussion as to treatment. I am aware of the fact that in most cases erythroplasia is said to eventuate in a malignant condition and that the most approved treatment is probably by endothermy. I should like to know, however, whether any of the members know of any cures by less radical methods. Endothermy would destroy sensation in the glans, and that is a serious matter for a young man.

DR. CHARLES MALLORY WILLIAMS: How long has any case of erythroplasia been followed? What is the longest duration on record?

DR. FRED WISE: This patient of Dr. Morse was examined also at the New York Post-Graduate Medical School and Hospital. I think I can answer some of the questions. The most important statement I wish to make is that I do not believe that roentgen rays, radium, curettage or the use of caustics such as trichloracetic acid or the acid solution of mercuric nitrate will cure the lesion. That has been my experience in two recent cases. I believe that thorough electrodesiccation, carried out at intervals rather than an attempt to cure the lesion all at one time, is the only method of treatment which has brought successful results so far. As to Dr. Williams' question, the first case of this condition I saw was that in a patient presented at a meeting of the Academy of Medicine with the diagnosis of erythroplasia of Queyrat, a name which was originally suggested by Dr. Goldenberg. This patient was not followed. The second case was in a patient who has been well for four or five months and has had no signs of recurrence. I think that any attempts to cure the lesion by methods other than electrodesiccation, unless a radical operation by ablation is performed, will prove to be futile and that electrodesiccation is probably the best remedy, despite the partial destruction of the glans penis.

DR. CHARLES MALLORY WILLIAMS: May I ask if there have been any records of untreated patients followed for a number of years?

DR. FRED WISE: As I recall, in the European literature the impression is that in all the patients who have not been treated the condition has turned out to be cancer.

DR. CHARLES MALLORY WILLIAMS: For how long were the patients followed?

DR. FRED WISE: I do not know how much time elapses before the lesions become cancerous. I do not know that this condition is regarded as a typical precancerosis.

DR. PAUL E. BECHET: I should like to ask Dr. Wise what the cosmetic results were.

DR. FRED WISE: The cosmetic results with electrodesiccation have been rather poor.

DR. HOWARD FOX: What about sensation after treatment?

DR. FRED WISE: I never asked the patients about cutaneous sensation after desiccation. They did not mention it, so I suppose that it was not much impaired.

One cannot tell much from only two cases, but the distortion of the glans is marked after desiccation. The treatment left ugly scars and quite a bit of deformity of the glans penis.

Dr. Howard Fox: Was the greater part of the glans involved in Dr. Wise's cases?

Dr. Fred Wise: Yes, it was.

Exhibition of Material and Books. Dr. Howard Fox.

I present a moulage of epithelioma which was made by Dr. F. Sokolow of the Bronner Institute for Venereal Diseases in Moscow.

I also exhibit the following old books on diseases of the skin: The works of Fracastorius, 1555; De morbis cutaneis by Mercurialis, 1572; Arcanismo Antigalico by Don Francisco, 1721; De morbis cutaneis by Daniel Turner, 1726; De morbis cutaneis by Johann Astruc, 1740; De morbis cutaneis by G. Cavelier, 1777; Histoire naturelle de la peau by J. B. Banau, 1802; A Treatise on the Venereal Disease by John Hunter, 1810; A Practical Treatise on Tinea Capitis Contagiosa and Its Cure by W. Cooks, 1810, A Practical Synopsis of Cutaneous Diseases by Thomas Bateman, 1816; Remarks on Cutaneous Diseases by J. H. Wilkinson, 1822; Diseases of the Skin by Arthur Clarke, 1828; Practical Synopsis of Cutaneous Diseases by Biett, 1832; Maladies de la peau by P. Roger, 1835; Practical Treatise on the Diseases of the Skin by Samuel Plumbe, 1837, and A. Cornelius Celsus of Medicine by James Greive, 1838.

Book Reviews

The Patient and the Weather. By William F. Petersen. Volume II. Price, $6.50. Pp. 530, with 249 figures and charts. Ann Arbor, Mich.: Edwards Brothers, Inc., 1934.

In a series of volumes of which this is the second, Dr. Petersen has undertaken to consider the highly difficult but important question of the influence of the weather on diseases. The question is difficult because one is dealing with imponderable factors which are extremely hard to evaluate. It is important because a large number of facts indicate that atmospheric conditions have effects on the healthy as well as on the diseased body. It is fortunate that Dr. Petersen has undertaken this investigation, for there is need for scientific consideration of the subject. He has brought to it a critical, trained, scientific mind, and even with these qualities he suggests much that is indefinite on the subject. To the dermatologist the special interest lies in the vascular disturbances of the skin which are considered from this standpoint. The two chapters given to this subject are extremely interesting and suggestive, and their reading by dermatologists will stimulate many ideas. But the book is of especial value for the realization which a general reading will give of the probable significance of the weather as a factor in the exciting of diseases and in the modification of their course. As Mark Twain said, "Everybody talks about the weather but nobody does anything about it." Dr. Petersen has distinctly done something about it. It is an ungrateful topic; the common reaction is to regard it slightingly. Dr. Petersen has taken it seriously; has given unending time and investigation and thought to the subject and, if he has not established, he has very strongly suggested, important facts in the pathogenesis of diseases. A debt of gratitude is due him.

Handbuch der Kinderheilkunde. Volume X. By M. von Pfaundler and A. Schlossmann. Price, 169 marks; bound, 178 marks. Pp. 884, with 383 illustrations. Leipzig: F. C. W. Vogel, 1935.

This tenth volume of the encyclopedia of children's diseases is a full consideration of cutaneous diseases in children. The first part, devoted to the principles of the subject—the anatomic structure of the skin in children, metabolism and immunobiology and general therapeutics—is the least complete of all. But in the next eight hundred and fifty pages is given a full consideration of all cutaneous diseases. Among the authors are many of the most distinguished dermatologists in Germany and Austria. The work is copiously illustrated with good pictures in black and white and has many colored illustrations which in their lifelike appearance could not be improved on. The work is a storehouse of knowledge in its field and would be a valuable addition to any physician's library.

Handbuch der Haut- und Geschlechtskrankheiten. Edited by J. Jadassohn. Volume XX, pt. 1. Price, 168 marks; bound, 176 marks. Pp. 920, with 98 illustrations. Berlin: Julius Springer, 1934.

This volume is concerned wholly with gonorrhea, so it does not come within the purview of dermatology, but it presents the subject with the detail, thoroughness and scholarship to which attention has been called so often in connection with this system.

Directory of Dermatologic Societies *

INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.
Place: Budapest, Hungary. Time: Sept. 15-21, 1935.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)
H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.
Place: Toronto, Ont. Time: May 1936.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY
Henry MacCormac, President, 23, Wimpole St., London, W. 1.
R. T. Brain, Secretary, 132, Harley St., London, W. 1.

NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY
Harry R. Foerster, Chairman, 208 E. Wisconsin Ave., Milwaukee.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: Kansas City, Mo. Time: May 11-15, 1936.

AMERICAN DERMATOLOGICAL ASSOCIATION
C. Guy Lane, President, 416 Marlboro St., Boston.
F. D. Weidman, Secretary, University of Pennsylvania, Philadelphia.

SECTIONAL DERMATOLOGIC SOCIETIES

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY
Joseph E. Gately, President, 1129 Calvert St., Baltimore.
Joseph V. Kennedy, Secretary, 1835 Eye St., Washington, D. C.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY
John R. Schermerhorn, President, 1225 Union St., Schenectady.
L. de Mello, Secretary-Treasurer, Medical Arts Bldg., Syracuse.

CENTRAL STATES DERMATOLOGICAL ASSOCIATION
Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: 1935.

IOWA AND WESTERN ILLINOIS DERMATOLOGICAL ASSOCIATION
J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.
Place: Iowa City. Time: Oct. 15, 1935.

NEW ENGLAND DERMATOLOGICAL SOCIETY
William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY
J. W. Roussel, Chairman, 150 Baronne St., New Orleans.
Cornelius F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

William H. Goeckerman, Chairman, 1680 N. Vine St., Hollywood.
Stanley O. Chambers, Secretary, 1210 Roosevelt Bldg., Los Angeles.

Florida Society of Dermatology and Syphilology

J. L. Kirby-Smith, Chairman, 204 Laura St, Jacksonville.
W. M. Sams, Secretary, 310 Ingram Bldg., Miami.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Louis Tulipan, Chairman, 224 E. 17th St., New York.
C. H. Peachey, Secretary, 197 S. Goodman St., Rochester.

Medical Society of the State of Pennsylvania Section on Dermatology

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Fred M. Jacob, Secretary, 7026 Jenkins Arcade Bldg., Pittsburgh.

Michigan State Medical Society, Section on Dermatology and Syphilology

A. R. Woodburne, Chairman, 26 Sheldon Ave., Grand Rapids.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

Minnesota Dermatological Society

Hamilton Montgomery, President, Mayo Clinic, Rochester.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma State Dermatological Society

C. L. Brundage, President, 1200 N. Walker St., Oklahoma City.
M. M. Wickham, Secretary, 716 W. Symmes St., Norman.

Texas Dermatological Society

J. C. Michael, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Austin.

LOCAL DERMATOLOGIC SOCIETIES

Atlanta Dermatological Society

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

Bronx Dermatological Society

Eugene F. Kelley, Chairman, 93 Radford St., Yonkers, N. Y.
Henry Silver, Secretary, 290 West End Ave., New York.

Brooklyn Dermatological Society

Jacob Skeer, President, 272 E. 19th St., Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

Buffalo-Rochester Dermatological Society

Albert R. McFarland, President, 315 Alexander St., Rochester, N. Y.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

Chicago Dermatological Society

William A. Pusey, President, 7 W. Madison St., Chicago.
Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

Cincinnati Dermatological Society

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

Cleveland Dermatological Society

H. G. Miskjian, President, 856 Rose Bldg., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

Detroit Dermatological Society

L. W. Shaffer, President, 1553 Woodward Ave, Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.
Place: Cincinnati, Ohio. Joint meeting with Central States Dermatological Association. Time: November, 1935.

Los Angeles Dermatological Society

N. P. Anderson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Thomas Nesbit, Secretary, 65 N. Madison Ave., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Paul E. Bechet, Chairman, 55 Park Ave., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Alberic Marin, President, 1414 Drummond St., Montreal, Canada.
Paul Poirier, Secretary, 2073 St. Denis St., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Max Scheer, Chairman, 509 Madison Ave., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

New York Dermatological Society

R. H. Rulison, Chairman, 145 E. 54th St., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

Omaha Dermatological Society

Charles McMartin, Chairman, 611 City National Bank Bldg., Omaha.
Donald J. Wilson, Secretary, 1216 Medical Arts Bldg., Omaha.

Philadelphia Dermatological Society

H. J. Smith, Chairman, Germantown Professional Bldg, Philadelphia.
Vaughn C. Garner, Secretary, Greene and Coulter Sts., Philadelphia.

Pittsburgh Dermatological Society

Bernhard A. Goldmann, President, Jenkins Arcade, Pittsburgh.
J. Cavanaugh, Secretary, 28 Market St., Youngstown, Ohio.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

L. R. Taussig, President, 384 Post St., San Francisco.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

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Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

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